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(54) **A Method of identifying unknown adeno-associated virus (AVV) sequences and a kit for the method**

Verfahren zur Identifizierung von Adeno-assoziiertem Virus (AAV) Sequenzen sowie Kit zur Ausführung der Methode

Une méthode d'identification de séquences de virus adéno-associés et kit permettant d'appliquer la méthode

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## Description

## BACKGROUND OF THE INVENTION

**[0001]** Adeno-associated virus (AAV), a member of the Parvovirus family, is a small nonenveloped, icosahedral virus with single-stranded linear DNA genomes of 4.7 kilobases (kb) to 6 kb. AAV is assigned to the genus, Dependovirus, because the virus was discovered as a contaminant in purified adenovirus stocks. AAV's life cycle includes a latent phase at which AAV genomes, after infection, are site specifically integrated into host chromosomes and an infectious phase in which, following either adenovirus or herpes simplex virus infection, the integrated genomes are subsequently rescued, replicated, and packaged into infectious viruses. The properties of non-pathogenicity, broad host range of infectivity, including non-dividing cells, and potential site-specific chromosomal integration make AAV an attractive tool for gene transfer.

**[0002]** Recent studies suggest that AAV vectors may be the preferred vehicle for gene therapy. To date, there have been 6 different serotypes of AAVs isolated from human or non-human primates (NHP) and well characterized. Among them, human serotype 2 is the first AAV that was developed as a gene transfer vector; it has been widely used for efficient gene transfer experiments in different target tissues and animal models. Gene therapy vectors based on adeno-associated virus type 1 have also been disclosed (Xiao et al. J. Virology; May 1999; pages 3994-4008). Clinical trials of the experimental application of AAV2 based vectors to some human disease models are in progress, and include such diseases as cystic fibrosis and hemophilia B.

**[0003]** A general PCR method suitable for detecting human papillomavirus types in cutaneous tumours and normal skin is known (Forslund et al J. of General Virology: 1999 80: P2437-2443).

**[0004]** What are desirable are AAV-based constructs for gene delivery.

## SUMMARY OF THE INVENTION

**[0005]** In one aspect, the invention provides a novel method of identifying unknown AAV sequences from cellular DNAs of various human and non-human primate (NHP) tissues using bioinformatics analysis, PCR based gene amplification and cloning technology, based on the nature of latency and integration of AAVs in the absence of helper virus co-infection, the method being defined in claim 1 hereinafter.

**[0006]** In another aspect the invention provides a kit for use in the method of the invention, the kit being as defined in claim 23 hereinafter.

## DETAILED DESCRIPTION OF THE INVENTION

**[0007]** In the present invention, the inventors have found a method which takes advantage of the ability of adeno-associated virus (AAV) to penetrate the nucleus, and, in the absence of a helper virus co-infection, to integrate into cellular DNA and establish a latent infection. This method utilizes a polymerase chain reaction (PCR)-based strategy for detection, identification of sequences of AAVs from DNAs from tissues of human and non-human primate origin as well as from other sources.

**[0008]** Nucleic acid sequences can be identified according to the method of the invention. One such adeno-associated virus is of the serotype, termed herein serotype 7 (AAV7). Other novel adeno-associated virus serotypes identified by the method include AAV10, AAV11, and AAV12.

**[0009]** Among particularly desirable AAV fragments which can be identified are the cap proteins, including the vp1, vp2, vp3, the hypervariable regions, the rep proteins, including rep 78, rep 68, rep 52, and rep 40, and the sequences encoding these proteins. Each of these fragments may be readily utilized in a variety of vector systems and host cells. Such fragments may be used alone, in combination with other AAV sequences or fragments, or in combination with elements from other AAV or non-AAV viral sequences. In one particularly desirable embodiment, a vector contains the AAV cap and/or rep sequences.

**[0010]** As described herein, alignments are performed using any of a variety of publicly or commercially available Multiple Sequence Alignment Programs, such as "Clustal W", accessible through Web Servers on the internet. Alternatively, Vector NTI utilities are also used. There are also a number of algorithms known in the art which can be used to measure nucleotide sequence identity, including those contained in the programs described above. As another example, polynucleotide sequences can be compared using Fasta, a program in GCG Version 6.1. Fasta provides alignments and percent sequence identity of the regions of the best overlap between the query and search sequences. For instance, percent sequence identity between nucleic acid sequences can be determined using Fasta with its default parameters (a word size of 6 and the NOPAM factor for the scoring matrix) as provided in GCG Version 6.1. Similar programs are available for amino acid sequences, e.g., the "Clustal X" program. Generally, any of these programs are used at default settings, although one of skill in the art can alter these settings as needed. Alternatively, one of skill in the art can utilize

another algorithm or computer program which provides at least the level of identity or alignment as that provided by the referenced algorithms and programs.

**[0011]** The term "substantial homology" or "substantial similarity," when referring to a nucleic acid, or fragment thereof, indicates that, when optimally aligned with appropriate nucleotide insertions or deletions with another nucleic acid (or its complementary strand), there is nucleotide sequence identity in at least about 95 to 99% of the aligned sequences. Preferably, the homology is over full-length sequence, or an open reading frame thereof, or another suitable fragment which is at least 15 nucleotides in length. Examples of suitable fragments are described herein.

**[0012]** The term "substantial homology" or "substantial similarity," when referring to amino acids or fragments thereof, indicates that, when optimally aligned with appropriate amino acid insertions or deletions with another amino acid, there is amino acid sequence identity in at least about 95 to 99% of the aligned sequences. Preferably, the homology is over full-length sequence, or a protein thereof, e.g., a cap protein, a rep protein, or a fragment thereof which is at least 8 amino acids, or more desirably, at least 15 amino acids in length. Examples of suitable fragments are described herein.

**[0013]** By the term "highly conserved" is meant at least 80% identity, preferably at least 90% identity, and more preferably, over 97% identity. Identity is readily determined by one of skill in the art by resort to algorithms and computer programs known by those of skill in the art.

**[0014]** The term "percent sequence identity" or "identical" in the context of nucleic acid sequences refers to the residues in the two sequences which are the same when aligned for maximum correspondence. The length of sequence identity comparison may be over the full-length of the genome, the full-length of a gene coding sequence, or a fragment of at least about 500 to 5000 nucleotides, is desired. However, identity among smaller fragments, e.g. of at least about nine nucleotides, usually at least about 20 to 24 nucleotides, at least about 28 to 32 nucleotides, at least about 36 or more nucleotides, may also be desired. Similarly, "percent sequence identity" may be readily determined for amino acid sequences, over the full-length of a protein, or a fragment thereof. Suitably, a fragment is at least about 8 amino acids in length, and may be up to about 700 amino acids. Examples of suitable fragments are described herein.

**[0015]** The AAV sequences and fragments thereof are useful in production of rAAV, and are also useful as antisense delivery vectors, gene therapy vectors, or vaccine vectors.

**[0016]** As described herein, the vectors containing the AAV capsid proteins are particularly well suited for use in applications in which the neutralizing antibodies diminish the effectiveness of other AAV serotype based vectors, as well as other viral vectors. The rAAV vectors are particularly advantageous in rAAV readministration and repeat gene therapy.

**[0017]** As used throughout this specification and the claims, the terms "comprising" and "including" and their variants are inclusive of other components, elements, integers, steps and the like. Conversely, the term "consisting" and its variants is exclusive of other components, elements, integers, steps and the like.

## I. Methods of the Invention

### A. Detection of Sequences Via Molecular Cloning

**[0018]** In one aspect, the invention provides a method of identifying target (unknown) nucleic acid sequences in a sample. This method is particularly well suited for detection of viral sequences which are integrated into the chromosome of a cell, e.g., adeno-associated viruses (AAV) and retroviruses, among others.

**[0019]** As used herein, a sample is any source containing nucleic acids, e.g., tissue, tissue culture, cells, cell culture, and biological fluids including, without limitation, urine and blood. These nucleic acid sequences may be DNA or RNA from plasmids, natural DNA or RNA from any source, including bacteria, yeast, viruses, and higher organisms such as plants or animals. DNA or RNA is extracted from the sample by a variety of techniques known to those of skill in the art, such as those described by Sambrook, *Molecular Cloning: A Laboratory Manual* (New York: Cold Spring Harbor Laboratory). The origin of the sample and the method by which the nucleic acids are obtained for application of the method of the invention is not a limitation of the present invention. Optionally, the method of the invention can be performed directly on the source of DNA, or on nucleic acids obtained (e.g., extracted) from a source.

**[0020]** The method of the invention involves subjecting a sample containing DNA to amplification via polymerase chain reaction (PCR) using a first set of primers specific for a first region of double-stranded nucleic acid sequences, thereby obtaining amplified sequences.

**[0021]** As used herein, each of the "regions" is predetermined based upon the alignment of the nucleic acid sequences of at least two serotypes (e.g., AAV) or strains (e.g., lentiviruses), and wherein each of said regions is composed of sequences having a 5' end which is highly conserved, a middle which is variable, and a 3' end which is highly conserved, each of these being conserved or variable relative to the sequences of at least AAV1-AAV6. The 5' and 3' ends are highly conserved over at least 18 base pairs (bp). However, one or both of the sequences at the 5' or 3' end may be conserved over more than 18 bp, more than 25 bp, more than 30 bp, or more than 50 bp at the 5' end. With respect to the variable region, there is no requirement for conserved sequences, these sequences may be relatively conserved, or may have less than 90, 80, or 70% identity among the aligned serotypes or strains.

**[0022]** Each of the regions may span about 100 bp to about 10 kilobase pairs in length, provided that the first region is at least 250 bp in length. However, it is particularly desirable that one of the regions is a "signature region", i.e., a region which is sufficiently unique to positively identify the amplified sequence as being from the target source. For example, in one embodiment, the first region is about 250 bp in length, and is sufficiently unique among known AAV sequences, that it positively identifies the amplified region as being of AAV origin. Further, the variable sequences within this region are sufficiently unique that can be used to identify the serotype from which the amplified sequences originate. Once amplified (and thereby detected), the sequences can be identified by performing conventional restriction digestion and comparison to restriction digestion patterns for this region in any of AAV1, AAV2, AAV3, AAV4, AAV5, or AAV6, or that of AAV7, AAV10, AAV11, AAV12, or any of the other novel serotypes identified by the invention, which is predetermined and provided by the present invention.

**[0023]** Given the guidance provided herein, one of skill in the art can readily identify such regions among other integrated viruses to permit ready detection and identification of these sequences. Thereafter, an optimal set of generic primers located within the highly conserved ends can be designed and tested for efficient amplification of the selected region from samples. This aspect of the invention is readily adapted to a diagnostic kit for detecting the presence of the target sequence (e.g., AAV) and for identifying the AAV serotype, using standards which include the restriction patterns for the AAV serotypes described herein or isolated using the techniques described herein. For example, quick identification or molecular serotyping of PCR products can be accomplished by digesting the PCR products and comparing restriction patterns.

**[0024]** Thus, in one embodiment, the "signature region" for AAV spans about bp 2800 to about 3200 of AAV 1 [SEQ ID NO:6], and corresponding base pairs in AAV 2, AAV3, AAV4, AAV5, and AAV6. More desirably, the region is about 250 bp, located within bp 2886 to about 3143 bp of AAV 1 [SEQ ID NO:6], and corresponding base pairs in AAV 2 [SEQ ID NO:7], AAV3 [SEQ ID NO:8], and other AAV serotypes. To permit rapid detection of AAV in the sample, primers which specifically amplify this signature region are utilized. However, the present invention is not limited to the exact sequences identified herein for the AAV signature region, as one of skill in the art may readily alter this region to encompass a shorter fragment, or a larger fragment of this signature region.

**[0025]** The PCR primers are generated using techniques known to those of skill in the art. Each of the PCR primer sets is composed of a 5' primer and a 3' primer. See, e.g., Sambrook et al, cited herein. The term "primer" refers to an oligonucleotide which acts as a point of initiation of synthesis when placed under conditions in which synthesis of a primer extension product which is complementary to a nucleic acid strand is induced. The primer is preferably single stranded. However, if a double stranded primer is utilized, it is treated to separate its strands before being used to prepare extension products. The primers may be about 15 to 25 or more nucleotides, and preferably at least 18 nucleotides. However, for certain applications shorter nucleotides, e.g., 7 to 15 nucleotides are utilized.

**[0026]** The primers are selected to be sufficiently complementary to the different strands of each specific sequence to be amplified to hybridize with their respective strands. Therefore, the primer sequence need not reflect the exact sequence of the region being amplified. For example, a non-complementary nucleotide fragment may be attached to the 5' end of the primer, with the remainder of the primer sequence being completely complementary to the strand. Alternatively, non-complementary bases or longer sequences can be interspersed into the primer, provided that the primer sequence has sufficient complementarity with the sequence of the strand to be amplified to hybridize therewith and form a template for synthesis of the extension product of the other primer.

**[0027]** The PCR primers for the signature region are based upon the highly conserved sequences of two or more aligned sequences (e.g., two or more AAV serotypes). The primers can accommodate less than exact identity among the two or more aligned AAV serotypes at the 5' end or in the middle. However, the sequences at the 3' end of the primers correspond to a region of two or more aligned AAV serotypes in which there is exact identity over at least five, preferably, over at least nine base pairs, and more preferably, over at least 18 base pairs at the 3' end of the primers. Thus, the 3' end of the primers is composed of sequences with 100% identity to the aligned sequences over at least five nucleotides. However, one can optionally utilize one, two, or more degenerate nucleotides at the 3' end of the primer.

**[0028]** For example, the primer set for the signature region of AAV was designed based upon a unique region within the AAV capsid, as follows. The 5' primer was based upon nt 2867-2891 of AAV2 [SEQ ID NO:7], 5'-GGTAATTCCTCCGGAATTGGCATT3'. The 3' primer was designed based upon nt 3096-3122 of AAV2 [SEQ ID NO:7], 5'-GACTCATCAACAACAAGTGGGATTC-3'. However, one of skill in the art may have readily designed the primer set based upon the corresponding regions of AAV 1, AAV3, AAV4, AAV5, AAV6, or based upon the information provided herein, AAV7, AAV10, AAV11, AAV12, or another novel AAV. In addition, still other primer sets can be readily designed to amplify this signature region, using techniques known to those of skill in the art.

## B. Isolation of Target Sequences

**[0029]** As described herein, the present invention uses a first primer set which specifically amplifies the signature region of the target sequence, e.g., an AAV serotype, in order to permit detection of the target. In a situation in which



further sequences are desired, e.g., if a novel AA V serotype is identified, the signature region may be extended. Thus, the invention may further utilize one or more additional primer sets.

**[0030]** Suitably, these primer sets are designed to include either the 5' or 3' primer of the first primer set and a second primer unique to the primer set, such that the primer set amplifies a region 5' or 3' to the signature region which anneals to either the 5' end or the 3' end of the signature region. For example, a first primer set is composed of a 5' primer, P1 and a 3' primer P2 to amplify the signature region. In order to extend the signature region on its 3' end, a second primer set is composed of primer P1 and a 3' primer P4, which amplifies the signature region and contiguous sequences downstream of the signature region. In order to extend the signature region on its 5' end, a third primer set is composed of a 5' primer, P5, and primer P2, such that the signature region and contiguous sequences upstream of the signature region are amplified. These extension steps are repeated (or performed at the same time), as needed or desired. Thereafter, the products results from these amplification steps are fused using conventional steps to produce an isolated sequence of the desired length.

**[0031]** The second and third primer sets are designed, as with the primer set for the signature region, to amplify a region having highly conserved sequences among the aligned sequences. Reference herein to the term "second" or "third" primer set is for each of discussion only, and without regard to the order in which these primers are added to the reaction mixture, or used for amplification. The region amplified by the second primer set is selected so that upon amplification it anneals at its 5' end to the 3' end of the signature region. Similarly, the region amplified by the third primer set is selected so that upon amplification it anneals at its 3' end to the 5' end of the signature region. Additional primer sets can be designed such that the regions which they amplify anneal to the either the 5' end or the 3' end of the extension products formed by the second or third primer sets, or by subsequent primer sets.

**[0032]** For example, where AAV is the target sequence, a first set of primers (P1 and P2) are used to amplify the signature region from the sample. In one desirable embodiment, this signature region is located within the AAV capsid. A second set of primers (P1 and P4) is used to extend the 3' end of the signature region to a location in the AAV sequence which is just before the AAV 3' ITR, i.e., providing an extension product containing the entire 3' end of the AAV capsid when using the signature region as an anchor. In one embodiment, the P4 primer corresponds to nt 4435 to 4462 of AAV2 [SEQ ID NO:7], and corresponding sequences in the other AAV serotypes. This results in amplification of a region of about 1.6 kb, which contains the 0.25 kb signature region. A third set of primers (P3 and P2) is used to extend the 5' end of signature region to a location in the AAV sequences which is in the 3' end of the rep genes, i.e., providing an extension product containing the entire 5' end of the AAV capsid when using the signature region as an anchor. In one embodiment, the P3 primer corresponds to nt 1384 to 1409 of AAV2 [SEQ ID NO:7], and corresponding sequences in the other AAV serotypes. This results in amplification of a region of about 1.7 kb, which contains the 0.25 kb signature region. Optionally, a fourth set of primers are used to further extend the extension product containing the entire 5' end of the AAV capsid to also include the rep sequences. In one embodiment, the primer designated P5 corresponds to nt 108 to 133 of AAV2 [SEQ ID NO:7], and corresponding sequences in the other AAV serotypes and is used in conjunction with the P2 primer.

**[0033]** Following completion of the desired number of extension steps, the various extension products are fused, making use of the signature region as an anchor or marker, to construct an intact sequence. In the example provided herein, AAV sequences containing, at a minimum, an intact AAV cap gene are obtained. Larger sequences may be obtained, depending upon the number of extension steps performed.

**[0034]** Suitably, the extension products are assembled into an intact AAV sequence using methods known to those of skill in the art. For example, the extension products may be digested with DralII, which cleaves at the DralII site located within the signature region, to provide restriction fragments which are re-ligated to provide products containing (at a minimum) an intact AAV cap gene. However, other suitable techniques for assembling the extension products into an intact sequence may be utilized. See, generally, Sambrook et al, cited herein.

**[0035]** As an alternative to the multiple extension steps described above, another embodiment of the invention provides for direct amplification of a 3.1 kb fragment which allows isolation of full-length cap sequences. To directly amplify a 3.1 kb full-length cap fragment from NHP tissue and blood DNAs, two other highly conserved regions were identified in AAV genomes for use in PCR amplification of large fragments. A primer within a conserved region located in the middle of the rep gene is utilized (AV1ns: 5' GCTGCGTCAACTGGACCAATGAGAAC 3', nt of SEQ ID NO:6) in combination with the 3' primer located in another conserved region downstream of the Cap gene (AV2cas: 5' CGCAGAGACCAAAGT-TCAACTGAAACGA 3', SEQ ID NO: 7) for amplification of AAV sequences including the full-length AAV cap. Typically, following amplification, the products are cloned and sequence analysis is performed with an accuracy of  $\geq 99.9\%$ . Using this method, the inventors have isolated at least 50 capsid clones which have subsequently been characterized. Among them, 37 clones were derived from Rhesus macaque tissues (rh.1 - rh.37), 6 clones from cynomolgous macaques (cy.1 - cy.6), 2 clones from Baboons (bb.1 and bb.2) and 5 clones from Chimps (ch.1 - ch.5). These clones are identified elsewhere in the specification, together with the species of animal from which they were identified and the tissues in that animal these novel sequences have been located.

## II. Diagnostic Kit

**[0036]** In another aspect, the invention provides a diagnostic kit as defined in claim 23 hereinafter for detecting the presence of an unknown adeno-associated virus (AAV) in a sample. Such a kit may contain a first set of 5' and 3' PCR primers specific for a signature region of the AAV nucleic acid sequence. Alternatively, or additionally, such a kit can contain a first set of 5' and 3' PCR primers specific for the 3.1 kb fragment which includes the full-length AAV capsid nucleic acid sequence identified herein (e.g., the AV1ns and AV2cas primers.) Optionally, a kit of the invention may further contain two or more additional sets of 5' and 3' primers, as described herein, and/or PCR probes. These primers and probes are used according to the present invention to amplify signature regions of each AAV serotype, e.g., using quantitative PCR.

**[0037]** Such a kit may further include one or more restriction enzymes, standards for AAV serotypes providing their "signature restriction enzyme digestions analyses", and/or other means for determining the serotype of the AAV detected.

**[0038]** In addition, kits of the invention may include, instructions, a negative and/or positive control, containers, diluents and buffers for the sample, indicator charts for signature comparisons, disposable gloves, decontamination instructions, applicator sticks or containers, and sample preparator cups, as well as any desired reagents, including media, wash reagents and concentration reagents. Such reagents may be readily selected from among the reagents described herein, and from among conventional concentration reagents. In one desirable embodiment, the wash reagent is an isotonic saline solution which has been buffered to physiologic pH, such as phosphate buffered saline (PBS); the elution reagent is PBS containing 0.4 M NaCl, and the concentration reagents and devices. For example, one of skill in the art will recognize that reagents such as polyethylene glycol (PEG), or  $\text{NH}_4\text{SO}_4$  may be useful, or that devices such as filter devices. For example, a filter device with a 100 K membrane would concentrate rAAV.

**[0039]** The kits provided by the present invention are useful for performing the methods described herein, and for study of biodistribution, epidemiology, mode of transmission of novel AAV serotypes in human and NHPs.

**[0040]** Thus, the methods and kits of the invention permit identification of target AAV sequences, particularly integrated AAV sequences.

**[0041]** In one notable example, the method of the invention facilitated analysis of cloned AAV sequences by the inventors, which revealed heterogeneity of proviral sequences between cloned fragments from different animals, all of which were distinct from the known six AAV serotypes, with the majority of the variation localized to hypervariable regions of the capsid protein. Surprising divergence of AAV sequences was noted in clones isolated from single tissue sources, such as lymph node, from an individual rhesus monkey. This heterogeneity is best explained by apparent evolution of AAV sequence within individual animals due, in part, to extensive homologous recombination between a limited number of co-infecting parenteral viruses. These studies suggest sequence evolution of widely disseminated virus during the course of a natural AAV infection that presumably leads to the formation of swarms of quasispecies which differ from one another in the array of capsid hypervariable regions. This is the first example of rapid molecular evolution of a DNA virus in a way that formerly was thought to be restricted to RNA viruses.

**[0042]** Sequences of several novel AAV serotypes identified by the method of the invention and characterization of these serotypes is provided.

## III. Novel AAV Serotypes

## A. Nucleic Acid Sequences

**[0043]** Nucleic acid sequences of novel AAV serotypes identified by the methods of the invention are provided. See, SEQ ID NO:1, 9 - 59, and 117 - 120. See also and the sequence listing.

**[0044]** For novel serotype AAV7, the full-length sequences, including the AAV 5' ITRs, capsid, rep, and AAV 3' ITRs are provided in SEQ ID NO:1.

**[0045]** For other novel AAV serotypes, the approximately 3.1 kb fragment isolated according to the method of the invention is provided. This fragment contains sequences encoding full-length capsid protein and all or part of the sequences encoding the rep protein. These sequences include the clones identified below.

**[0046]** For still other novel AAV serotypes, the signature region encoding the capsid protein is provided. For example, the AAV10 nucleic acid sequences include those illustrated in See, SEQ ID NO:117, which spans 255 bases. The AAV11 nucleic acid sequences include the DNA sequences illustrated in SEQ ID NO:118 which spans 258 bases. The AAV12 nucleic acid sequences include the DNA sequences illustrated in SEQ ID NO: 119, which consists of 255 bases. Using the methodology described above, further AAV10, AAV11 and AAV 12 sequences can be readily identified and used for a variety of purposes, including those described for AAV7 and the other novel serotypes herein.

**[0047]** Novel NHP sequences identified by the invention include those provided in the following Table I, which are identified by clone number:

Table 1

AAV Cap Sequence	Clone Number	Source		
		Species	Tissue	SEQ ID NO (DNA)
Rh.1	Clone 9 (AAV9)	Rhesus	Heart	5
Rh.2	Clone 43.1	Rhesus	MLN	39
Rh.3	Clone 43.5	Rhesus	MLN	40
Rh.4	Clone 43.12	Rhesus	MLN	41
Rh.5	Clone 43.20	Rhesus	MLN	42
Rh.6	Clone 43.21	Rhesus	MLN	43
Rh.7	Clone 43.23	Rhesus	MLN	44

Table 1 (cont'd)

Rh.8	Clone 43.25	Rhesus	MLN	45
Rh.9	Clone 44.1	Rhesus	Liver	46
Rh.10	Clone 44.2	Rhesus	Liver	59
Rh.11	Clone 44.5	Rhesus	Liver	47
Rh.12	Clone 42.1B	Rhesus	MLN	30
Rh.13	42.2	Rhesus	MLN	9
Rh.14	Clone 42.3A	Rhesus	MLN	32
Rh.15	Clone 42.3B	Rhesus	MLN	36
Rh.16	Clone 42.4	Rhesus	MLN	33
Rh.17	Clone 42.5A	Rhesus	MLN	34
Rh.18	Clone 42.5B	Rhesus	MLN	29
Rh.19	Clone 42.6B	Rhesus	MLN	38
Rh.20	Clone 42.8	Rhesus	MLN	27
Rh.21	Clone 42.10	Rhesus	MLN	35
Rh.22	Clone 42.11	Rhesus	MLN	37
Rh.23	Clone 42.12	Rhesus	MLN	58
Rh.24	Clone 42.13	Rhesus	MLN	31
Rh.25	Clone 42.15	Rhesus	MLN	28
Rh.26	Clone 223.2	Rhesus	Liver	49
Rh.27	Clone 223.4	Rhesus	Liver	50
Rh.28	Clone 223.5	Rhesus	Liver	51
Rh.29	Clone 223.6	Rhesus	Liver	52
Rh.30	Clone 223.7	Rhesus	Liver	53
Rh.31	Clone 223.10	Rhesus	Liver	48
Rh.32	Clone C1	Rhesus	Spleen, Duo, Kid & Liver	19
Rh.33	Clone C3	Rhesus		20
Rh.34	Clone C5	Rhesus		21
Rh.35	Clone F1	Rhesus	Liver	22
Rh.36	Clone F3	Rhesus		23
Rh.37	Clone F5	Rhesus		24
Cy.1	Clone 1.3	Cyno	Blood	14
Cy.2	Clone 13.3B	Cyno	Blood	15
Cy.3	Clone 24.1	Cyno	Blood	16
Cy.4	Clone 27.3	Cyno	Blood	17
Cy.5	Clone 7.2	Cyno	Blood	18
Cy.6	Clone 16.3	Cyno	Blood	10

Table 1 (cont'd)

bb.1	Clone 29.3	Baboon	Blood	11
bb.2	Clone 29.5	Baboon	Blood	13
Ch.1	Clone A3.3	Chimp	Blood	57
Ch.2	Clone A3.4	Chimp	Blood	54
Ch.3	Clone A3.5	Chimp	Blood	55
Ch.4	Clone A3.7	Chimp	Blood	56

**[0048]** A novel NHP clone was made by splicing capsids fragments of two chimp adenoviruses into an AAV2 rep construct. This new clone, A3.1, is also termed Ch.5 [SEQ ID NO:20]. Additionally, the present invention includes two human AAV sequences, termed H6 [SEQ ID NO:25] and H2 [SEQ ID NO:26].

**[0049]** The AAV nucleic acid sequences further encompass the strand which is complementary to the strands provided in the sequences provided in the Sequence Listing [SEQ ID NO:1, 9 - 59, 117-120], nucleic acid sequences, as well as the RNA and cDNA sequences corresponding to the sequences provided in the Sequence Listing [SEQ ID NO:1, 9 - 59, 117-120], and their complementary strands. Also included in the nucleic acid sequences are natural variants and engineered modifications of the sequences of the Sequence Listing [SEQ ID NO:1, 9 - 59, 117-120], and their complementary strands. Such modifications include, for example, labels which are known in the art, methylation, and substitution of one or more of the naturally occurring nucleotides with a degenerate nucleotide.

**[0050]** Further included are nucleic acid sequences which are greater than 85%, preferably at least about 90%, more preferably at least about 95%, and most preferably at least about 98 to 99% identical or homologous to the sequences of the invention, including the Sequence Listing [SEQ ID NO:1, 9 - 59, 117-120]. These terms are as defined herein.

**[0051]** Also included are fragments of the novel AAV sequences identified by the method described herein. Suitable fragments are at least 15 nucleotides in length, and encompass functional fragments, i.e., fragments which are of biological interest. In one embodiment, these fragments are fragments of the novel sequences of the Sequence Listing [SEQ ID NO:1, 9 - 59, 117-120], their complementary strands, cDNA and RNA complementary thereto.

**[0052]** Examples of suitable fragments are provided with respect to the location of these fragments on AAV1, AAV2, or AAV7. However, using the alignment provided herein (obtained using the Clustal W program at default settings), or similar techniques for generating an alignment with other novel serotypes of the invention, one of skill in the art can readily identify the precise nucleotide start and stop codons for desired fragments.

**[0053]** Examples of suitable fragments include the sequences encoding the three variable proteins (vp) of the AAV capsid which are alternative splice variants: vp1 [e.g., nt 825 to 3049 of AA V7, SEQ ID NO: 1]; vp2 [e.g., nt 1234 - 3049 of AAV7, SEQ ID NO: 1]; and vp 3 [e.g., nt 1434 - 3049 of AAV7, SEQ ID NO:1]. It is notable that AAV7 has an unusual GTG start codon. With the exception of a few house-keeping genes, such a start codon has not previously been reported in DNA viruses. The start codons for vp1, vp2 and vp3 for other AAV serotypes have been believed to be such that they permit the cellular mechanism of the host cell in which they reside to produce vp1, vp2 and vp3 in a ratio of 10%:10%:80%, respectively, in order to permit efficient assembly of the virion. However, the AAV7 virion has been found to assemble efficiently even with this rare GTG start codon. Thus, the inventors anticipate this it is desirable to alter the start codon of the vp3 of other AAV serotypes to contain this rare GTG start codon, in order to improve packaging efficiency, to alter the virion structure and/or to alter location of epitopes (e.g., neutralizing antibody epitopes) of other AAV serotypes. The start codons may be altered using conventional techniques including, e.g., site directed mutagenesis. The altered AAV virions may be of any selected serotype, composed of a vp 3, and/or optionally, vp 1 and/or vp2 having start codons altered to GTG.

**[0054]** Other suitable fragments of AAV, include a fragment containing the start codon for the AAV capsid protein [e.g., nt 468 to 3090 of AAV7, SEQ ID NO:1, nt 725 to 3090 of AAV7, SEQ ID NO: 1, and corresponding regions of the other AAV serotypes]. Still other fragments of AAV7 and the other novel AAV semtypes identified using the methods described herein include those encoding the rep proteins, including *rep* 78 [e.g., initiation codon 334 for AAV7], *rep* 68 [initiation codon nt 334 for AAV7], *rep* 52 [initiation codon 1006 for AAV7], and *rep* 40 [initiation codon 1006 for AAV7]. Other fragments of interest may include the AAV 5' inverted terminal repeats ITRs, [nt 1 to 107 for AAV7]; the AA V 3' ITRs [nt 4704 to 4721 for AAV7], P19 sequences. AAV P40 sequences, the rep binding site, and the terminal resolute site (TRS). Still other suitable fragments will be readily apparent to those of skill in the art.

**[0055]** In addition to the nucleic acid sequences provided in the figures and Sequence Listing, there are nucleic acid molecules and sequences which are designed to express the amino acid sequences, proteins and peptides of the AAV serotypes of the invention. These include nucleic acid sequences which encode the following novel AAV amino acid sequences: C1 [SEQ ID NO:60], C2 [SEQ ID NO:61], C5 [SEQ ID NO:62], A3-3 [SEQ ID NO:66], A3-7 [SEQ ID NO:67],

A3-4 [SEQ ID NO:68], A3-5 [SEQ ID NO: 69], 3.3b [SEQ ID NO: 62], 223.4 [SEQ ID NO: 73], 223-5 [SEQ ID NO:74], 223-10 [SEQ ID NO:75], 223-2 [SEQ ID NO:76], 223-7 [SEQ ID NO: 77], 223-6 [SEQ ID NO: 78], 44-1 [SEQ ID NO: 79], 44-5 [SEQ ID NO:80], 44-2 [SEQ ID NO:81], 42-15 [SEQ ID NO: 84], 42-8 [SEQ ID NO: 85], 42-13 [SEQ ID NO:86], 42-3A [SEQ ID NO:87], 42-4 [SEQ ID NO:88], 42-5A [SEQ ID NO:89], 42-1B [SEQ ID NO:90], 42-5B [SEQ ID NO:91], 43-1 [SEQ ID NO: 92], 43-12 [SEQ ID NO: 93], 43-5 [SEQ ID NO:94], 43-21 [SEQ ID NO:96], 43-25 [SEQ ID NO: 97], 43-20 [SEQ ID NO:99], 24.1 [SEQ ID NO: 101], 42.2 [SEQ ID NO:102], 7.2 [SEQ ID NO: 103], 27.3 [SEQ ID NO: 104], 16.3 [SEQ ID NO: 105], 42.10 [SEQ ID NO: 106], 42-38 [SEQ ID NO: 107], 42-11 [SEQ ID NO: 108], F1 [SEQ ID NO: 109], F5 [SEQ ID NO: 110], F3 [SEQ ID NO:111], 42-6B [SEQ ID NO: 112], and/or 42-12 [SEQ ID NO: 113], and artificial AAV serotypes generated using these sequences and/or unique fragments thereof.

**[0056]** As used herein, artificial AAV serotypes include, without limitation, AAV with a non-naturally occurring capsid protein. Such an artificial capsid may be generated by any suitable technique, using a novel AAV sequence (e.g., a fragment of a vp1 capsid protein) in combination with heterologous sequences which may be obtained from another AAV serotype (known or novel), non-contiguous portions of the same AAV serotype, from a non-AAV viral source, or from a non-viral source. An artificial AAV serotype may be, without limitation, a chimeric AAV capsid, a recombinant AAV capsid, or a "humanized" AAV capsid.

#### B. AAV Amino Acid Sequences, Proteins and Peptides

**[0057]** The invention provides proteins and fragments thereof which are encoded by the nucleic acid sequences of the novel AAV serotypes identified herein, including, e.g., AA V7 [nt 825 to 3049 of AA V7, SEQ ID NO: 1] the other novel serotypes provided herein. Thus, the capsid proteins of the novel serotypes of the invention, including: H6 [SEQ ID NO: 25], H2 [SEQ ID NO: 26], 42-2 [SEQ ID NO:9], 42-8 [SEQ ID NO:27], 42-15 [SEQ ID NO:28], 42-5b [SEQ ID NO: 29], 42-1b [SEQ ID NO:30], 42-13 [SEQ ID NO: 31], 42-3a [SEQ ID NO: 32], 42-4 [SEQ ID NO:33], 42-5a [SEQ ID NO: 34], 42-10 [SEQ ID NO:35], 42-3b [SEQ ID NO: 36], 42-11 [SEQ ID NO: 37], 42-6b [SEQ ID NO:38], 43-1 [SEQ ID NO: 39], 43-5 [SEQ ID NO: 40], 43-12 [SEQ ID NO:41], 43-20 [SEQ ID NO:42], 43-21 [SEQ ID NO: 43], 43-23 [SEQ ID NO:44], 43-25 [SEQ ID NO: 45], 44.1 [SEQ ID NO:47], 44.5 [SEQ ID NO:47], 223.10 [SEQ ID NO:48], 223.2 [SEQ ID NO:49], 223.4 [SEQ ID NO:50], 223.5 [SEQ ID NO:51], 223.6 [SEQ ID NO: 52], 223.7 [SEQ ID NO: 53], A3.4 [SEQ ID NO: 54], A3.5 [SEQ ID NO:55], A3.7 [SEQ ID NO: 56], A3.3 [SEQ ID NO:57], 42.12 [SEQ ID NO: 58], and 44.2 [SEQ ID NO: 59], can be readily generated using conventional techniques from the open reading frames provided for the above-listed clones.

**[0058]** The sequences, proteins, and fragments may be produced by any suitable means, including recombinant production, chemical synthesis, or other synthetic means. Such production methods are within the knowledge of those of skill in the art.

#### IV. Production of rAAV with novel AAV capsids

**[0059]** Novel, wild-type AAV serotypes can be identified by the invention, the sequences of which wild-type AAV serotypes are free of DNA and/or cellular material with these viruses are associated in nature. In another aspect, the present invention provides molecules which utilize the novel AAV sequences of the invention, including fragments thereof, for production of molecules useful in delivery of a heterologous gene or other nucleic acid sequences to a target cell.

**[0060]** The following examples illustrate several aspects and embodiments of the invention.

#### EXAMPLES

Example 1: PCR amplification, cloning and characterization of novel AAV sequences.

**[0061]** Tissues from nonhuman primates were screened for AAV sequences using a PCR method based on oligonucleotides to highly conserved regions of known AAVs. A stretch of AAV sequence spanning 2886 to 3143 bp of AAV1 [SEQ ID NO:6] was selected as a PCR amplicon in which a hypervariable region of the capsid protein (Cap) that is unique to each known AAV serotype, which is termed herein a "signature region," is flanked by conserved sequences. In later analysis, this signature region was shown to be located between conserved residues spanning hypervariable region 3.

**[0062]** An initial survey of peripheral blood of a number of nonhuman primate species revealed detectable AAV in a subset of animals from species such as rhesus macaques, cynomolgous macaques, chimpanzees and baboons. However, there were no AAV sequences detected in some other species tested, including Japanese macaques, pig-tailed macaques and squirrel monkeys. A more extensive analysis of vector distribution was conducted in tissues of rhesus monkeys of the University of Pennsylvania and Tulane colonies recovered at necropsy. This revealed AAV sequence throughout a wide array of tissues.

## A. Amplification of an AAV signature region

**[0063]** DNA sequences of AAV1-6 and AAVs isolated from Goose and Duck were aligned to each other using "Clustal W" at default settings. Sequence similarities among AAVs were compared.

**[0064]** In the line of study, a 257 bp region spanning 2886 bp to 3143 bp of AAV 1 [SEQ ID NO: 6], and the corresponding region in the genomes of AAV 2-6 genomes was identified by the inventors. This region is located with the AAV capsid gene and has highly conserved sequences among at both 5' and 3' ends and is relatively variable sequence in the middle. In addition, this region contains a *DraIII* restriction enzyme site (CACCACGTC, SEQ ID NO:15). The inventors have found that this region serves as specific signature for each known type of AAV DNA. In other words, following PCR reactions, digestion with endonucleases that are specific to each known serotypes and gel electrophoresis analysis, this regions can be used to definitively identify amplified DNA as being from serotype 1, 2, 3, 4, 5, 6, or another serotype.

**[0065]** The primers were designed, validated and PCR conditions optimized with AAV1, 2 and 5 DNA controls. The primers were based upon the sequences of AAV2: 5' primer, 1S: bp 2867-2891 of AAV2 (SEQ ID NO:7) and 3' primer, 18as, bp 3095-3121 of AAV2 (SEQ ID NO:7).

**[0066]** Cellular DNAs from different tissues including blood, brain, liver, lung, testis, etc. of different rhesus monkeys were studied utilizing the strategy described above. The results revealed that DNAs from different tissues of these monkeys gave rise to strong PCR amplifications. Further restriction analyses of PCR products indicated that they were amplified from AAV sequences different from any published AAV sequences.

**[0067]** PCR products (about 255 bp in size) from DNAs of a variety of monkey tissues have been cloned and sequenced. Bioinformatics study of these novel AAV sequences indicated that they are novel AAV sequences of capsid gene and distinct from each other. Multiple sequence alignment analysis was performed using the Clustal W (1.81) program. The percentage of sequence identity between the signature regions of AAV 1-7 and AAV 10-12 genomes is provided below.

Table 1. Sequences for Analysis

Sequence #	AAV Serotype	Size (bp)
1	AAV1	258
2	AAV2	255
3	AAV3	255
4	AAV4	246
5	AAV5	258
6	AAV6	258
7	AAV7	258
10	AAV10	255
11	AAV11	258
12	AAV12	255

Table 3. Pairwise Alignment (Percentage of Identity)

	AAV2	AAV3	AAV4	AAV5	AAV6	AAV7	AAV10	AAV11	AAV12
AAV1	90	90	81	76	97	91	93	94	93
AAV2		93	79	78	90	90	93	93	92
AAV3			80	76	90	92	92	92	92
AAV4				76	81	84	82	81	79
AAV5					75	78	79	79	76
AAV6						91	92	94	94
AAV7							94	92	92
AAV10								95	93

Table continued

	AAV2	AAV3	AAV4	AAV5	AAV6	AAV7	AAV10	AAV11	AAV12
AAV11									94

**[0068]** Over 300 clones containing novel AAV serotype sequences that span the selected 257 bp region were isolated and sequenced. Bioinformatics analysis of these 300+ clones suggests that this 257 bp region is critical in serving as a good land marker or signature sequence for quick isolation and identification of novel AAV serotype.

#### B. Use of the signature region for PCR amplification.

**[0069]** The 257 bp signature region was used as a PCR anchor to extend PCR amplifications to 5' of the genome to cover the junction region of rep and cap genes (1398 bp - 3143 bp, SEQ ID NO:6) and 3' of the genome to obtain the entire cap gene sequence (2866 bp - 4600 bp, SEQ ID NO:6). PCR amplifications were carried out using the standard conditions, including denaturing at 95°C for 0.5-1 min, annealing at 60-65°C for 0.5-1 min and extension at 72°C for 1 min per kb with a total number of amplification cycles ranging from 28 to 42.

**[0070]** Using the aligned sequences as described in "A", two other relative conserved regions were identified in the sequence located in 3' end of rep genes and 5' to the 257 bp region and in the sequence down stream of the 257 bp fragment but before the AAV' 3 ITR. Two sets of new primers were designed and PCR conditions optimized for recovery of entire capsid and a part of rep sequences of novel AAV serotypes. More specifically, for the 5' amplification, the 5' primer, AV1Ns, was GCTGCGTCAACTGGACCAATGAGAAC [nt 1398-1423 of AAV1, SEQ ID NO:6] and the 3' primer was 18as, identified above. For the 3' amplification, the 5' primer was 1s, identified above, and the 3' primer was AV2Las, TCGTTTCAGTTGAACCTTGGTCTCTGCG [nt 4435-4462 of AAV2, SEQ ID NO:7].

**[0071]** In these PCR amplifications, the 257 bp region was used as a PCR anchor and land marker to generate overlapping fragments to construct a complete capsid gene by fusion at the DraIII site in the signature region following amplification of the 5' and 3' extension fragments obtained as described herein. More particularly, to generate the intact AAV7 cap gene, the three amplification products (a) the sequences of the signature region; (b) the sequences of the 5' extension; and (c) the sequences of the 3' extension were cloned into a pCR4-Topo [Invitrogen] plasmid backbone according to manufacturer's instructions. Thereafter, the plasmids were digested with DraIII and recombined to form an intact cap gene.

**[0072]** In this line of work, about 80 % of capsid sequences of AAV7 and AAV 8 were isolated and analyzed. Another novel serotype, AAV9, was also discovered from Monkey #2.

**[0073]** Using the PCR conditions described above, the remaining portion of the rep gene sequence for AAV7 is isolated and cloned using the primers that amplify 108 bp to 1461 bp of AAV genome (calculated based on the numbering of AAV2, SEQ ID NO:7). This clone is sequenced for construction of a complete AAV7 genome without ITRs.

#### C. Direct Amplification of 3.1 kb Cap fragment

**[0074]** To directly amplify a 3.1 kb full-length Cap fragment from NHP tissue and blood DNAs, two other highly conserved regions were identified in AAV genomes for use in PCR amplification of large fragments. A primer within a conserved region located in the middle of the rep gene was selected (AV1ns: 5' GCTGCGTCAACTGGACCAATGAGAAC 3', nt 1398-1423 of SEQ ID NO:6) in combination with the 3' primer located in another conserved region downstream of the Cap gene (AV2cas: 5' CGCAGAGACCAAAGTTCAACTGAAACGA 3', SEQ ID NO:7) for amplification of full-length cap fragments. The PCR products were Topo-cloned according to manufacturer's directions (Invitrogen) and sequence analysis was performed by Qiagen Genomics (Qiagen Genomics, Seattle, WA) with an accuracy of ≥ 99.9%. A total of 50 capsid clones were isolated and characterized. Among them, 37 clones were derived from Rhesus macaque tissues (rh.1 - rh.37), 6 clones from cynomolgous macaques (cy.1 - cy.6), 2 clones from Baboons (bb.1 and bb.2) and 5 clones from Chimps (ch.1 - ch.5).

**[0075]** To rule out the possibility that sequence diversity within the novel AAV family was not an artifact of the PCR, such as PCR-mediated gene splicing by overlap extension between different partial DNA templates with homologous sequences, or the result of recombination process in bacteria, a series of experiments were performed under identical conditions for VP1 amplification using total cellular DNAs. First, intact AAV7 and AAV8 plasmids were mixed at an equal molar ratio followed by serial dilutions. The serially diluted mixtures were used as templates for PCR amplification of 3.1 kb VP1 fragments using universal primers and identical PCR conditions to that were used for DNA amplifications to see whether any hybrid PCR products were generated. The mixture was transformed into bacteria and isolated transformants to look for hybrid clones possibly derived from recombination process in bacterial cells. In a different experiment, we restricted AAV7 and AAV8 plasmids with Msp I, Ava I and HaeI, all of which cut both genomes multiple times at different



positions, mixed the digestions in different combinations and used them for PCR amplification of VP1 fragments under the same conditions to test whether any PCR products could be generated through overlap sequence extension of partial AAV sequences. In another experiment, a mixture of gel purified 5' 1.5 kb AAV7 VP1 fragment and 3' 1.7 kb AAV8 VP1 fragment with overlap in the signature region was serially diluted and used for PCR amplification in the presence and absence of 200 ng cellular DNA extracted from a monkey cell line that was free of AAV sequences by TaqMan analysis. None of these experiments demonstrated efficient PCR-mediated overlap sequence production under the conditions of the genomic DNA Cap amplification (data not shown). As a further confirmation, 3 pairs of primers were designed, which were located at different HVRs, and were sequence specific to the variants of clone 42s from Rhesus macaque F953, in different combinations to amplify shorter fragments from mesenteric lymph node (MLN) DNA from F953 from which clone 42s were isolated. All sequence variations identified in full-length Cap clones were found in these short fragments (data not shown).

#### Example 2: Adeno-Associated Viruses Undergo Substantial Evolution in Primates During Natural Infections

**[0076]** Sequence analysis of selected AAV isolates revealed divergence throughout the genome that is most concentrated in hypervariable regions of the capsid proteins. Epidemiologic data indicate that all known serotypes are endemic to primates, although isolation of clinical isolates has been restricted to AAV2 and AAV3 from anal and throat swabs of human infants and AAV5 from a human condylomatous wart. No known clinical sequelae have been associated with AAV infection.

**[0077]** In an attempt to better understand the biology of AAV, nonhuman primates were used as models to characterize the sequelae of natural infections. Tissues from nonhuman primates were screened for AAV sequences using the PCR method of the invention based on oligonucleotides to highly conserved regions of known AAVs (see Example 1). A stretch of AAV sequence spanning 2886 to 3143 bp of AAV1 [SEQ ID NO:6] was selected as a PCR amplicon in which conserved sequences are flanked by a hypervariable region that is unique to each known AAV serotype, termed herein a "signature region."

**[0078]** An initial survey of peripheral blood of a number of nonhuman primate species including rhesus monkeys, cynomolgous monkeys, chimpanzees, and baboons revealed detectable AAV in a subset of animals from all species. A more extensive analysis of vector distribution was conducted in tissues of rhesus monkeys of the University of Pennsylvania and Tulane colonies recovered at necropsy. This revealed AAV sequence throughout a wide array of tissues.

**[0079]** The amplified signature sequences were subcloned into plasmids and individual transformants were subjected to sequence analysis. This revealed substantial variation in nucleotide sequence of clones derived from different animals. Variation in the signature sequence was also noted in clones obtained within individual animals. Tissues harvested from two animals in which unique signature sequences were identified (i.e., colon from 98E044 and heart from 98E056) were further characterized by expanding the sequence amplified by PCR using oligonucleotides to highly conserved sequences. In this way, complete proviral structures were reconstructed for viral genomes from both tissues as described herein. These proviruses differ from the other known AAVs with the greatest sequence divergence noted in regions of the Cap gene.

**[0080]** Additional experiments were performed to confirm that AAV sequences resident to the nonhuman primate tissue represented proviral genomes of infectious virus that is capable of being rescued and form virions. Genomic DNA from liver tissue of animal 98E056, from which AAV8 signature sequence was detected, was digested with an endonuclease that does not have a site within the AAV sequence and transfected into 293 cells with a plasmid containing an E1 deleted genome of human adenovirus serotype 5 as a source of helper functions. The resulting lysate was passaged on 293 cells once and the lysate was recovered and analyzed for the presence of AAV Cap proteins using a broadly reacting polyclonal antibody to Cap proteins and for the presence and abundance of DNA sequences from the PCR amplified AAV provirus from which AAV8 was derived. Transfection of endonuclease restricted heart DNA and the adenovirus helper plasmid yielded high quantities of AAV8 virus as demonstrated by the detection of Cap proteins by Western blot analysis and the presence of  $10^4$  AAV8 vector genomes per 293 cell. Lysates were generated from a large-scale preparation and the AAV was purified by cesium sedimentation. The purified preparation demonstrated 26 nm icosahedral structures that look identical to those of AAV serotype 2. Transfection with the adenovirus helper alone did not yield AAV proteins or genomes, ruling out contamination as a source of the rescued AAV.

**[0081]** To further characterize the inter and intra animal variation of AAV signature sequence, selected tissues were subjected to extended PCR to amplify entire Cap open reading frames.

**[0082]** The resulting fragments were cloned into bacterial plasmids and individual transformants were isolated and fully sequenced. This analysis involved mesenteric lymph nodes from three rhesus monkeys (Tulane/V223 - 6 clones; Tulane/T612 - 7 clones; Tulane/F953 - 14 clones), liver from two rhesus monkeys (Tulane/V251 - 3 clones; Penn/00E033 - 3 clones), spleen from one rhesus monkey (Penn/97E043 - 3 clones), heart from one rhesus monkey (IHGT/98E046 - 1 clone) and peripheral blood from one chimpanzee (New Iberia/X133 - 5 clones), six cynomolgous macaques (Charles River/A1378, A3099, A3388, A3442, A2821, A3242 - 6 clones total) and one Baboon (SFRB/8644 - 2 clones). Of the

50 clones that were sequenced from 15 different animals, 30 were considered non-redundant based on the finding of at least 7 amino acid differences from one another. The non-redundant VP1 clones are numbered sequentially as they were isolated, with a prefix indicating the species of non-human primate from which they were derived. The structural relationships between these 30 non-redundant clones and the previously described 8 AAV serotypes were determined using the SplitsTree program [Huson, D. H. SplitsTree: analyzing and visualizing evolutionary data. *Bioinformatics* **14**, 68-73 (1998)] with implementation of the method of split decomposition. The analysis depicts homoplasy between a set of sequences in a tree-like network rather than a bifurcating tree. The advantage is to enable detection of groupings that are the result of convergence and to exhibit phylogenetic relationships even when they are distorted by parallel events. Extensive phylogenetic research will be required in order to elucidate the AAV evolution, whereas the intention here only is to group the different clones as to their sequence similarity.

**[0083]** To confirm that the novel VP1 sequences were derived from infectious viral genomes, cellular DNA from tissues with high abundance of viral DNA was restricted with an endonuclease that should not cleave within AAV and transfected into 293 cells, followed by infection with adenovirus. This resulted in rescue and amplification of AAV genomes from DNA of tissues from two different animals (data not shown).

**[0084]** VP1 sequences of the novel AAVs were further characterized with respect to the nature and location of amino acid sequence variation. All 30 VP1 clones that were shown to differ from one another by greater than 1% amino acid sequence were aligned and scored for variation at each residue. An algorithm developed to determine areas of sequence divergence yielded 12 hypervariable regions (HVR) of which 5 overlap or are part of the 4 previously described variable regions [Kotin, cited above; Rutledge, cited above]. The threefold-proximal peaks contain most of the variability (HVR5-10). Interestingly the loops located at the 2 and 5 fold axis show intense variation as well. The HVRs 1 and 2 occur in the N-terminal portion of the capsid protein that is not resolved in the X-ray structure suggesting that the N-terminus of the VP1 protein is exposed on the surface of the virion.

**[0085]** Real-time PCR was used to quantify AAV sequences from tissues of 21 rhesus monkeys using primers and probes to highly conserved regions of Rep (one set) and Cap (two sets) of known AAVs. Each data point represents analysis from tissue DNA from an individual animal. This confirmed the wide distribution of AAV sequences, although the quantitative distribution differed between individual animals. The source of animals and previous history or treatments did not appear to influence distribution of AAV sequences in rhesus macaques. The three different sets of primers and probes used to quantify AAV yielded consistent results. The highest levels of AAV were found consistently in mesenteric lymph nodes at an average of 0.01 copies per diploid genome for 13 animals that were positive. Liver and spleen also contained high abundance of virus DNA. There were examples of very high AAV, such as in heart of rhesus macaque 98E056, spleen of rhesus macaque 97E043 and liver of rhesus macaque RQ4407, which demonstrated 1.5, 3 and 20 copies of AAV sequence per diploid genome respectively. Relatively low levels of virus DNA were noted in peripheral blood mononuclear cells, suggesting the data in tissue are not due to resident blood components (data not shown). It should be noted that this method would not necessarily capture all AAVs resident to the nonhuman primates since detection requires high homology to both the oligonucleotides and the real time PCR probe. Tissues from animals with high abundance AAV DNA was further analyzed for the molecular state of the DNA, by DNA hybridization techniques, and its cellular distribution, by *in situ* hybridization.

**[0086]** The kind of sequence variation revealed in AAV proviral fragments isolated from different animals and within tissues of the same animals is reminiscent of the evolution that occurs for many RNA viruses during pandemics or even within the infection of an individual. In some situations the notion of a wild-type virus has been replaced by the existence of swarms of quasispecies that evolve as a result of rapid replication and mutations in the presence of selective pressure. One example is infection by HIV, which evolves in response to immunologic and pharmacologic pressure. Several mechanisms contribute to the high rate of mutations in RNA viruses, including low fidelity and lack of proof reading capacity of reverse transcriptase and non-homologous and homologous recombination.

**[0087]** Evidence for the formation of quasispecies of AAV was illustrated in this study by the systematic sequencing of multiple cloned proviral fragments. In fact, identical sequences could not be found within any extended clones isolated between or within animals. An important mechanism for this evolution of sequence appears to be a high rate of homologous recombination between a more limited number of parenteral viruses. The net result is extensive swapping of hypervariable regions of the Cap protein leading to an array of chimeras that could have different tropisms and serologic specificities (i.e., the ability to escape immunologic responses especially as it relates to neutralizing antibodies). Mechanisms by which homologous recombination could occur are unclear. One possibility is that + and - strands of different single stranded AAV genomes anneal during replication as has been described during high multiplicity of infections with AAV recombinants. It is unclear if other mechanisms contribute to sequence evolution in AAV infections. The overall rate of mutation that occurs during AAV replication appears to be relatively low and the data do not suggest high frequencies of replication errors. However, substantial rearrangements of the AAV genome have been described during lytic infection leading to the formation of defective interfering particles. Irrespective of the mechanisms that lead to sequence divergence, with few exceptions, vp1 structures of the quasispecies remained intact without frameshifts or nonsense mutations suggesting that competitive selection of viruses with the most favorable profile of fitness contribute to the population

dynamics.

**[0088]** These studies have implications in several areas of biology and medicine. The concept of rapid virus evolution, formerly thought to be a property restricted to RNA viruses, should be considered in DNA viruses, which classically have been characterized by serologic assays. It will be important in terms of parvoviruses to develop a new method for describing virus isolates that captures the complexity of its structure and biology, such as with HIV, which are categorized as general families of similar structure and function called Clades. An alternative strategy is to continue to categorize isolates with respect to serologic specificity and develop criteria for describing variants within serologic groups.

Example 3: Vectorology of recombinant AAV genomes equipped with AAV2 ITRs using chimeric plasmids containing AAV2 rep and novel AAV cap genes for serological and gene transfer studies in different animal models.

**[0089]** Chimeric packaging constructs are generated by fusing AAV2 rep with cap sequences of novel AAV serotypes. These chimeric packaging constructs are used, initially, for pseudotyping recombinant AAV genomes carrying AAV2 ITRs by triple transfection in 293 cell using Ad5 helper plasmid. These pseudotyped vectors are used to evaluate performance in transduction-based serological studies and evaluate gene transfer efficiency of novel AAV serotypes in different animal models including NHP and rodents, before intact and infectious viruses of these novel serotypes are isolated.

#### A. *pAAV2GFP*

**[0090]** The AAV2 plasmid which contains the AAV2 ITRs and green fluorescent protein expressed under the control of a constitutive promoter. This plasmid contains the following elements: the AAV2 ITRs, a CMV promoter, and the GFP coding sequences.

#### B. *Cloning of trans plasmid*

**[0091]** To construct the chimeric trans-plasmid for production of recombinant pseudotyped AAV7 vectors, p5E18 plasmid (Xiao *et al.*, 1999, *J. Virol* **73**:3994-4003) was partially digested with Xho I to linearize the plasmid at the Xho I site at the position of 3169 bp only. The Xho I cut ends were then filled in and ligated back. This modified p5E18 plasmid was restricted with Xba I and Xho I in a complete digestion to remove the AAV2 cap gene sequence and replaced with a 2267 bp Spe I/Xho I fragment containing the AAV7 cap gene which was isolated from pCRAAV7 6-5+15-4 plasmid.

**[0092]** The resulting plasmid contains the AAV2 rep sequences for Rep78/68 under the control of the AAV2 P5 promoter, and the AAV2 rep sequences for Rep52/40 under the control of the AAV2 P19 promoter. The AAV7 capsid sequences are under the control of the AAV2 P40 promoter, which is located within the Rep sequences. This plasmid further contains a spacer 5' of the rep ORF.

#### C. *Production of Pseudotyped rAAV*

**[0093]** The rAAV particles (AAV2 vector in AAV7 capsid) are generated using an adenovirus-free method. Briefly, the cis plasmid (pAAV2.1 lacZ plasmid containing AAV2 ITRs), and the trans plasmid pCRAAV7 6-5+15-4 (containing the AAV2 rep and AAV7 cap) and a helper plasmid, respectively, were simultaneously co-transfected into 293 cells in a ratio of 1:1:2 by calcium phosphate precipitation.

**[0094]** For the construction of the pAd helper plasmids, pBG 10 plasmid was purchased from Microbix (Canada). A RsrII fragment containing L2 and L3 was deleted from pBHG10, resulting in the first helper plasmid, pAdΔF13. Plasmid AdΔ F1 was constructed by cloning Asp700/Sall fragment with a PmeI/Sgfl deletion, isolating from pBHG10, into Blue-script. MLP, L2, L2 and L3 were deleted in the pAdΔF1. Further deletions of a 2.3 kb NruI fragment and, subsequently, a 0.5 kb RsrII/NruI fragment generated helper plasmids pAdΔF5 and pAdΔF6, respectively. The helper plasmid, termed pΔF6, provides the essential helper functions of E2a and E4 ORF6 not provided by the E1-expressing helper cell, but is deleted of adenoviral capsid proteins and functional E1 regions).

**[0095]** Typically, 50 μg of DNA (cis:trans:helper) was transfected onto a 150 mm tissue culture dish. The 293 cells were harvested 72 hours post-transfection, sonicated and treated with 0.5% sodium deoxycholate (37°C for 10 min.) Cell lysates were then subjected to two rounds of a CsCl gradient. Peak fractions containing rAAV vector are collected, pooled and dialyzed against PBS.

Example 4: Creation of infectious clones carrying intact novel AAV serotypes for study of basic virology in human and NHP derived cell lines and evaluation of pathogenesis of novel AAV serotypes in NHP and other animal models.

**[0096]** To achieve this goal, the genome walker system is employed to obtain 5' and 3' terminal sequences (ITRs)

and complete construction of clones containing intact novel AAV serotype genomes.

**[0097]** Briefly, utilizing a commercially available Universal Genome Walker Kit [Clontech], genomic DNAs from monkey tissues or cell lines that are identified as positive for the presence of AAV7 sequence are digested with Dra I, EcoR V, Pvu II and Stu I endonucleases and ligated to Genome Walker Adaptor to generate 4 individual Genome Walker Libraries (GWLs). Using DNAs from GWLs as templates, AAV7 and adjacent genomic sequences will be PCR-amplified by the adaptor primer 1 (API, provided in the kit) and an AAV7 specific primer 1, followed by a nested PCR using the adaptor primer 2 (AP2) and another AAV7 specific primer 2, both of which are internal to the first set of primers. The major PCR products from the nested PCR are cloned and characterized by sequencing analysis.

**[0098]** In this experiment, the primers covering the 257 bp or other signature fragment of a generic AAV genome are used for PCR amplification of cellular DNAs extracted from Human and NHP derived cell lines to identify and characterize latent AAV sequences. The identified latent AAV genomes are rescued from the positive cell lines using adenovirus helpers of different species and strains.

**[0099]** To isolate infectious AAV clones from NHP derived cell lines, a desired cell line is obtained from ATCC and screened by PCR to identify the 257 bp amplicon, i.e., signature region of the invention. The 257 bp PCR product is cloned and serotyped by sequencing analysis. For these cell lines containing the AAV7 sequence, the cells are infected with SV-15, a simian adenovirus purchased from ATCC, human Ad5 or transfected with plasmid construct housing the human Ad genes that are responsible for AAV helper functions. At 48 hour post infection or transfection, the cells are harvested and Hirt DNA is prepared for cloning of AAV7 genome following Xiao et al., 1999, J. Virol, 73:3994-4003.

#### Example 5 - Production of AAV Vectors

**[0100]** A pseudotyping strategy similar to that of Example 3 for AAV1/7 was employed to produce AAV2 vectors packaged with AAV1, AAV5 and AAV8 capsid proteins. Briefly, recombinant AAV genomes equipped with AAV2 ITRs were packaged by triple transfection of 293 cells with cis-plasmid, adenovirus helper plasmid and a chimeric packaging construct where the AAV2 rep gene is fused with cap genes of novel AAV serotypes. To create the chimeric packaging constructs, the Xho I site of p5E18 plasmid at 3169 bp was ablated and the modified plasmid was restricted with Xba I and Xho I in a complete digestion to remove the AAV2 cap gene and replace it with a 2267 bp Spe I/Xho I fragment containing the AAV8 cap gene [Xiao, W., et al., (1999) *J Virol* **73**, 3994-4003]. A similar cloning strategy was used for creation of chimeric packaging plasmids of AAV2/1 and AAV2/5. All recombinant vectors were purified by the standard CsCl<sub>2</sub> sedimentation method except for AAV2/2, which was purified by single step heparin chromatography.

**[0101]** Genome copy (GC) titers of AAV vectors were determined by TaqMan analysis using probes and primers targeting SV40 poly A region as described previously [Gao, G., et al., (2000) *Hum Gene Ther* **11**, 2079-91].

**[0102]** Vectors were constructed for each serotype for a number of *in vitro* and *in vivo* studies. Eight different transgene cassettes were incorporated into the vectors and recombinant virions were produced for each serotype. The recovery of virus, based on genome copies, is summarized in Table 4 below. The yields of vector were high for each serotype with no consistent differences between serotypes. Data presented in the table are average genome copy yields with standard deviation x 10<sup>13</sup> of multiple production lots of 50 plate (150 mm) transfections.

**Table 4. Production of Recombinant Vectors**

	AAV2/1	AAV2/2	AAV2/5	AAV2/7	AAV2/8
<b>CMV LacZ</b>	7.30 ± 4.33 (n=9)	4.49 ± 2.89 (n=6)	5.19 ± 5.19 (n=8)	3.42 (n=1)	0.87 (n=1)
<b>CMV EGFP</b>	6.43 ± 2.42 (n=2)	3.39 ± 2.42 (n=2)	5.55 ± 6.49 (n=4)	2.98 ± 2.66 (n=2)	3.74 ± 3.88 (n=2)
<b>TBG LacZ</b>	4.18 (n=1)	0.23 (n=1)	0.704 ± 0.43 (n=2)	2.16 (n=1)	0.532 (n=1)
<b>Alb A1AT</b>	4.67 ± 0.75 (n=2)	4.77 (n=1)	4.09 (n=1)	5.04 (n=1)	2.02 (n=1)
<b>CB A1AT</b>	0.567 (n=1)	0.438 (n=1)	2.82 (n=1)	2.78 (n=1)	0.816 ± 0.679 (n=2)
<b>TBG rhCG</b>	8.51 ± 6.65 (n=6)	3.47 ± 2.09 (n=5)	5.26 ± 3.85 (n=4)	6.52 ± 3.08 (n=4)	1.83 ± 0.98 (n=5)
<b>TBG cFIX</b>	1.24 ± 1.29 (n=3)	0.63 ± 0.394 (n=6)	3.74 ± 2.48 (n=7)	4.05 (n=1)	15.8 ± 15.0 (n=5)

#### Example 6 - Serologic Analysis of Pseudotyped Vectors

**[0103]** C57BL/6 mice were injected with vectors of different serotypes of AAVCBA1AT vectors intramuscularly (5 x

10<sup>11</sup> GC) and serum samples were collected 34 days later. To test neutralizing and cross-neutralizing activity of sera to each serotype of AAV, sera was analyzed in a transduction based neutralizing antibody assay [Gao, G. P., et al., (1996) *J Virol* **70**, 8934-43]. More specifically, the presence of neutralizing antibodies was determined by assessing the ability of serum to inhibit transduction of 84-31 cells by reporter viruses (AAVCMVEGFP) of different serotypes. Specifically, the reporter virus AAVCMVEGFP of each serotype [at multiplicity of infection (MOI) that led to a transduction of 90% of indicator cells] was pre-incubated with heat-inactivated serum from animals that received different serotypes of AAV or from naïve mice. After 1-hour incubation at 37° C, viruses were added to 84-31 cells in 96 well plates for 48 or 72- hour, depending on the virus serotype. Expression of GFP was measured by Fluorolmagin (Molecular Dynamics) and quantified by Image Quant Software. Neutralizing antibody titers were reported as the highest serum dilution that inhibited transduction to less than 50%.

[0104] The availability of GFP expressing vectors simplified the development of an assay for neutralizing antibodies that was based on inhibition of transduction in a permissive cell line (i.e., 293 cells stably expressing E4 from Ad5). Sera to selected AAV serotypes were generated by intramuscular injection of the recombinant viruses. Neutralization of AAV transduction by 1:20 and 1:80 dilutions of the antisera was evaluated (See Table 5 below). Antisera to AAV1, AAV2, AAV5 and AAV8 neutralized transduction of the serotype to which the antiserum was generated (AAV5 and AAV8 to a lesser extent than AAV1 and AAV2) but not to the other serotype (i.e., there was no evidence of cross neutralization suggesting that AAV 8 is a truly unique serotype).

Table 5. Serological Analysis of New AAV Serotypes.

		% Infection on 84-31 cells with AAVCMVEGFP virus:									
		AAV2/1		AAV2/2		AAV2/5		AAV2/7		AAV2/8	
		Serum dilution:		Serum dilution:		Serum dilution:		Serum dilution:		Serum dilution:	
Sera:	Immunization Vector	1/20	1/80	1/20	1/80	1/20	1/80	1/20	1/80	1/20	1/80
Group 1	AAV2/1	0	0	100	100	100	100	100	100	100	100
Group 2	AAV2/2	100	100	0	0	100	100	100	100	100	100
Group 3	AAV2/5	100	100	100	100	16.5	16.5	100	100	100	100
Group 4	AAV2/7	100	100	100	100	100	100	61.5	100	100	100
Group 5	AAV2/8	100	100	100	100	100	100	100	100	26.3	60

[0105] Human sera from 52 normal subjects were screened for neutralization against selected serotypes. No serum sample was found to neutralize AAV2/7 and AAV2/8 while AAV2/2 and AAV2/1 vectors were neutralized in 20% and 10% of sera, respectively. A fraction of human pooled IgG representing a collection of 60,000 individual samples did not neutralize AAV2/7 and AAV2/8, whereas AAV2/2 and AAV2/1 vectors were neutralized at titers of serum equal to 1/1280 and 1/640, respectively.

#### Example 7 - *In vivo* Evaluation of Different Serotypes of AAV Vectors

[0106] In this study, 7 recombinant AAV genomes, AAV2CBhA1AT, AAV2AlbA1AT, AAV2CMVrhCG, AAV2TBGrhCG, AAV2TBGcFIX, AAV2CMVLacZ and AAV2TBGLacZ were packaged with capsid proteins of different serotypes. In all 7 constructs, minigene cassettes were flanked with AAV2 ITRs. cDNAs of human  $\alpha$ -antitrypsin (A1AT) [Xiao, W., et al., (1999) *J Virol* **73**, 3994-4003]  $\beta$ -subunit of rhesus monkey choriogonadotropic hormone (CG) [Zoltick, P. W. & Wilson, J. M. (2000) *Mol Ther* **2**, 657-9] canine factor IX [Wang, L., et al., (1997) *Proc Natl Acad Sci USA* **94**, 11563-6] and bacterial  $\beta$ -galactosidase (i.e., Lac Z) genes were used as reporter genes. For liver-directed gene transfer, either mouse albumin gene promoter (Alb) [Xiao, W. (1999), cited above] or human thyroid hormone binding globulin gene promoter (TBG) [Wang (1997), cited above] was used to drive liver specific expression of reporter genes. In muscle-directed gene transfer experiments, either cytomegalovirus early promoter (CMV) or chicken  $\beta$ -actin promoter with CMV enhancer (CB) was employed to direct expression of reporters.

[0107] For muscle-directed gene transfer, vectors were injected into the right tibialis anterior of 4-6 week old NCR nude or C57BL/6 mice (Taconic, Germantown, NY). In liver-directed gene transfer studies, vectors were infused intraportally into 7-9 week old NCR nude or C57BL/6 mice (Taconic, Germantown, NY). Serum samples were collected intraorbitally at different time points after vector administration. Muscle and liver tissues were harvested at different time points for cryosectioning and Xgal histochemical staining from animals that received the lacZ vectors. For the re-administration experiment, C56BL/6 mice initially received AAV2/1, 2/2, 2/5, 2/7 and 2/8CBhA1AT vectors intramuscularly and followed for A1AT gene expression for 7 weeks. Animals were then treated with AAV2/8TBGcFIX intraportally and studied for cFIX gene expression.

[0108] ELISA based assays were performed to quantify serum levels of hA1AT, rhCG and cFIX proteins as described previously [Gao, G. P., et al., (1996) *J Virol* **70**, 8934-43; Zoltick, P. W. & Wilson, J. M. (2000) *Mol Ther* **2**, 657-9; Wang, L., et al., *Proc Natl Acad Sci U S A* **94**, 11563-6]. The experiments were completed when animals were sacrificed for harvest of muscle and liver tissues for DNA extraction and quantitative analysis of genome copies of vectors present in target tissues by TaqMan using the same set of primers and probe as in titration of vector preparations [Zhang, Y., et al., (2001) *Mol Ther* **3**, 697-707].

[0109] The performance of vectors base on the new serotypes were evaluated in murine models of muscle and liver-directed gene transfer and compared to vectors based on the known serotypes AAV1, AAV2 and AAV5. Vectors expressing secreted proteins (alpha-antitrypsin (A1AT) and chorionic gonadotropin (CG)) were used to quantitate relative transduction efficiencies between different serotypes through ELISA analysis of sera. The cellular distribution of transduction within the target organ was evaluated using lacZ expressing vectors and X-gal histochemistry.

[0110] The performance of AAV vectors in skeletal muscle was analyzed following direct injection into the tibialis anterior muscles. Vectors contained the same AAV2 based genome with the immediate early gene of CMV or a CMV enhanced  $\beta$ -actin promoter driving expression of the transgene. Previous studies indicated that immune competent C57BL/6 mice elicit limited humoral responses to the human A1AT protein when expressed from AAV vectors [Xiao, W., et al., (1999) *J Virol* **73**, 3994-4003].

[0111] In each strain, AAV2/1 vector produced the highest levels of A1AT and AAV2/2 vector the lowest, with AAV2/7 and AAV2/8 vectors showing intermediate levels of expression. Peak levels of CG at 28 days following injection of nu/nu NCR mice showed the highest levels from AAV2/7 and the lowest from AAV2/2 with AAV2/8 and AAV2/1 in between. Injection of AAV2/1 and AAV2/7 lacZ vectors yielded gene expression at the injection sites in all muscle fibers with substantially fewer lacZ positive fibers observed with AAV2/2 and AAV 2/8 vectors. These data indicate that the efficiency of transduction with AA V2/7 vectors in skeletal muscle is similar to that obtained with AAV2/1, which is the most efficient in skeletal muscle of the previously described serotypes [Xiao, W. (1999), cited above; Chao, H., et al., (2001) *Mol Ther* **4**, 217-22; Chao, H., et al., (2000) *Mol Ther* **2**, 619-23].

[0112] Similar murine models were used to evaluate liver-directed gene transfer. Identical doses of vector based on genome copies were infused into the portal veins of mice that were analyzed subsequently for expression of the transgene. Each vector contained an AAV2 based genome using previously described liver-specific promoters (i.e., albumin or thyroid hormone binding globulin) to drive expression of the transgene. More particularly, CMVCG and TBGCG minigene cassettes were used for muscle and liver-directed gene transfer, respectively. Levels of rhCG were defined as relative units (RUs  $\times 10^3$ ). The data were from assaying serum samples collected at day 28, post vector administration (4 animals per group). As shown in Table 3, the impact of capsid proteins on the efficiency of transduction of A1AT vectors in nu/nu and C57BL/6 mice and CG vectors in C57BL/6 mice was consistent (See Table 6).

**Table 6. Expression of  $\beta$ -unit of Rhesus Monkey Chorionic Gonadotropin (rhCG)**

Vector	Muscle	Liver
AAV2/1	4.5 $\pm$ 2.1	1.6 $\pm$ 1.0
AAV2	0.5 $\pm$ 0.1	0.7 $\pm$ 0.3
AAV2/5	ND*	4.8 $\pm$ 0.8
AAV2/7	14.2 $\pm$ 2.4	8.2 $\pm$ 4.3
AAV2/8	4.0 $\pm$ 0.7	76.0 $\pm$ 22.8

\* Not determined in this experiment.

[0113] In all cases, AAV2/8 vectors yielded the highest levels of transgene expression that ranged from 16 to 110 greater than what was obtained with AAV2/2 vectors; expression from AAV2/5 and AAV2/7 vectors was intermediate with AAV2/7 higher than AAV2/5. Analysis of X-Gal stained liver sections of animals that received the corresponding lacZ vectors showed a correlation between the number of transduced cells and overall levels of transgene expression. DNAs extracted from livers of C57BL/6 mice who received the A1AT vectors were analyzed for abundance of vector DNA using real time PCR technology.

[0114] The amount of vector DNA found in liver 56 days after injection correlated with the levels of transgene expression (See Table 7). For this experiment, a set of probe and primers targeting the SV40 polyA region of the vector genome was used for TaqMan PCR. Values shown are means of three individual animals with standard deviations. The animals were sacrificed at day 56 to harvest liver tissues for DNA extraction. These studies indicate that AAV8 is the most efficient vector for liver-directed gene transfer due to increased numbers of transduced hepatocytes.

**Table 7 - Real Time PCR Analysis for Abundance of AAV Vectors in nu/nu Mouse Liver Following Injection of 1x10<sup>11</sup> Genome Copies of Vector.**

AAV vectors/Dose	Genome Copies per Cell
AAV2/1A1bA1AT	0.6 ± 0.36
AAV2A1bA1AT	0.003 ± 0.001
AAV2/5A1bA1AT	0.83 ± 0.64
AAV2/7A1bA1AT	2.2 ± 1.7
AAV2/8A1bA1AT	18 ± 11

**[0115]** The serologic data described above suggest that AAV2/8 vector should not be neutralized *in vivo* following immunization with the other serotypes. C57BL/6 mice received intraportal injections of AAV2/8 vector expressing canine factor IX (10<sup>11</sup> genome copies) 56 days after they received intramuscular injections of A1AT vectors of different serotypes. High levels of factor IX expression were obtained 14 days following infusion of AAV2/8 into naïve animals (17±2 µg/ml, n=4) which were not significantly different that what was observed in animals immunized with AAV2/1 (31±23 µg/ml, n=4), AAV2/2 (16 µg/ml, n=2), and AAV2/7 (12 µg/ml, n=2). This contrasts to what was observed in AAV2/8 immunized animals that were infused with the AAV2/8 factor IX vector in which no detectable factor IX was observed (< 0.1 µg/ml, n=4).

**[0116]** Oligonucleotides to conserved regions of the cap gene did amplify sequences from rhesus monkeys that represented unique AAVs. Identical cap signature sequences were found in multiple tissues from rhesus monkeys derived from at least two different colonies. Full-length rep and cap open reading frames were isolated and sequenced from single sources. Only the cap open reading frames of the novel AAVs were necessary to evaluate their potential as vectors because vectors with the AAV7 or AAV8 capsids were generated using the ITRs and rep from AAV2. This also simplified the comparison of different vectors since the actual vector genome is identical between different vector serotypes. In fact, the yields of recombinant vectors generated using this approach did not differ between serotypes.

**[0117]** Vectors based on AAV7 and AAV8 appear to be immunologically distinct (i.e., they are not neutralized by antibodies generated against other serotypes). Furthermore, sera from humans do not neutralize transduction by AAV7 and AAV8 vectors, which is a substantial advantage over the human derived AAVs currently under development for which a significant proportion of the human population has pre-existing immunity that is neutralizing [Chirmule, N., et al., (1999) *Gene Ther* 6, 1574-83].

**[0118]** The tropism of each new vector is favorable for *in vivo* applications. AAV2/7 vectors appear to transduce skeletal muscle as efficiently as AAV2/1, which is the serotype that confers the highest level of transduction in skeletal muscle of the primate AAVs tested to date [Xiao, W., cited above; Chou (2001), cited above, and Chou (2000), cited above]. Importantly, AAV2/8 provides a substantial advantage over the other serotypes in terms of efficiency of gene transfer to liver that until now has been relatively disappointing in terms of the numbers of hepatocytes stably transduced. AAV2/8 consistently achieved a 10 to 100-fold improvement in gene transfer efficiency as compared to the other vectors. The basis for the improved efficiency of AAV2/8 is unclear, although it presumably is due to uptake via a different receptor that is more active on the basolateral surface of hepatocytes. This improved efficiency will be quite useful in the development of liver-directed gene transfer where the number of transduced cells is critical, such as in urea cycle disorders and familial hypercholesterolemia.

**[0119]** Thus, the present invention provides a novel approach for isolating new AAVs based on PCR retrieval of genomic sequences. The amplified sequences were easily incorporated into vectors and tested in animals. The lack of pre-existing immunity to AAV7 and the favorable tropism of the vectors for muscle indicates that AAV7 is suitable for use as a vector in human gene therapy and other *in vivo* applications. Similarly, the lack of pre-existing immunity to the AAV serotypes of the invention, and their tropisms, renders them useful in delivery of therapeutic molecules and other useful molecules.

#### Example 9 - Tissue Tropism Studies

**[0120]** In the design of a high throughput functional screening scheme for novel AAV constructs, a non-tissue specific and highly active promoter, CB promoter (CMV enhanced chicken β actin promoter) was selected to drive an easily detectable and quantifiable reporter gene, human α anti-trypsin gene. Thus only one vector for each new AAV clone needs to be made for gene transfer studies targeting 3 different tissues, liver, lung and muscle to screen for tissue tropism of a particular AAV construct. The following table summarizes data generated from 4 novel AAV vectors in the tissue tropism studies (AAVCBA1AT), from which a novel AAV capsid clone, 44.2, was found to be a very potent gene transfer vehicle in all 3 tissues with a big lead in the lung tissue particularly. Table 8 reports data obtained (in µg A1AT/mL serum) at day 14 of the study.

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Table 8

Vector	Target Tissue		
	Lung	Liver	Muscle
AAV2/1	ND	ND	45±11
AAV2/5	0.6±0.2	ND	ND
AAV2/8	ND	84±30	ND
AAV2/rh.2 (43.1)	14±7	25±7.4	35±14
AAV2/rh.10 (44.2)	23±6	53±19	46±11
AAV2/rh.13 (42.2)	3.5±2	2±0.8	3.5±1.7
AAV2/rh.21 (42.10)	3.1±2	2±1.4	4.3±2

A couple of other experiments were then performed to confirm the superior tropism of AAV 44.2 in lung tissue. First, AAV vector carried CC10hA1AT minigene for lung specific expression were pseudotyped with capsids of novel AAVs were given to Immune deficient animals (NCR nude) in equal volume (50 µl each of the original preps without dilution) via intratracheal injections as provided in the following table. In Table 9, 50 µl of each original prep per mouse, NCR Nude, detection limit ≥0.033 µg/ml, Day 28

Table 9

Vector	Total GC in 50 µl vector	µg of A1AT/ml with 50µl vector	µg of A1AT/ml with 1x10 <sup>11</sup> vector	Relative Gene transfer as compared to rh.10 (clone 44.2)
2/1	3x10 <sup>12</sup>	2.6±0.5	0.09±0.02	2.2
2/2	5.5x10 <sup>11</sup>	<0.03	<0.005	<0.1
2/5	3.6x10 <sup>12</sup>	0.65±0.16	0.02±0.004	0.5
2/7	4.2x10 <sup>12</sup>	1±0.53	0.02±0.01	0.5
2/8	7.5x10 <sup>11</sup>	0.9±0.7	0.12±0.09	2.9
2/ch.5 (A.3.1)	9x10 <sup>12</sup>	1±0.7	0.01±0.008	0.24
2/rh.8 (43.25)	4.6x10 <sup>12</sup>	26±21	0.56±0.46	13.7
2/rh.10 (44.2)	2.8x10 <sup>12</sup>	115±38	4.1±1.4	100
2/rh.13 (42.2)	6x10 <sup>12</sup>	7.3±0.8	0.12±0.01	2.9
2/rh.21 (42.10)	2.4x10 <sup>12</sup>	9±0.9	0.38±0.04	9.3
2/rh.22 (42.11)	2.6x10 <sup>12</sup>	6±0.4	0.23±0.02	5.6
2/rh.24 (42.13)	1.1x10 <sup>11</sup>	0.4±0.3	0.4±0.3	1

The vectors were also administered to immune competent animals (C57BL/6) in equal genome copies (1x10<sup>11</sup> GC) as shown in the Table 10. (1x10<sup>11</sup> GC per animal, C57BL/6, day 14, detection limit ≥0.033 µg/ml)

Table 10

AAV Vector	µg of A1AT/ml with 1x10 <sup>11</sup> vector	Relative Gene transfer as compared to rh.10 (clone 44.2)
2/1	0.076±0.031	2.6
2/2	0.1±0.09	3.4
2/5	0.084±0.033	2.9



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Table continued

AAV Vector	$\mu\text{g of A1AT/ml with } 1 \times 10^{11} \text{ vector}$	Relative Gene transfer as compared to rh.10 (clone 44.2)
2/7	$0.33 \pm 0.01$	11
2/8	$1.92 \pm 1.3$	2.9
2/ch.5 (A.3.1)	$0.048 \pm 0.004$	1.6
2/rh.8 (43.25)	$1.7 \pm 0.7$	58
2/rh.10 (44.2)	$2.93 \pm 1.7$	100
2/rh.13 (42.2)	$0.45 \pm 0.15$	15
2/rh.21 (42.10)	$0.86 \pm 0.32$	29
2/rh.22 (42.11)	$0.38 \pm 0.18$	13
2/rh.24 (42.13)	$0.3 \pm 0.19$	10

[0121] The data from both experiments confirmed the superb tropism of clone 44.2 in lung-directed gene transfer.

[0122] Interestingly, performance of clone 44.2 in liver and muscle directed gene transfer was also outstanding, close to that of the best liver transducer, AAV8 and the best muscle transducer AAV1, suggesting that this novel AAV has some intriguing biological significance.

[0123] To study serological properties of those novel AAVs, pseudotyped AAVGFP vectors were created for immunization of rabbits and in vitro transduction of 84-31 cells in the presence and absence of antisera against different capsids. The data are summarized below:

Table 11a. Cross-NAB assay in 8431 cells and adenovirus (Adv) coinfection Infection in 8431 cells (coinfecting with Adv) with:

Serum from rabbit immunized with:	$10^9$ GC	$10^9$ GC	$10^9$ GC	$10^{10}$ GC
	<b>rh.13</b>	<b>rh.21</b>	<b>rh.22</b>	<b>rh.24</b>
	AAV2/42.2	AAV2/42.10	AAV2/42.1	AAV2/42.13
AAV2/1	1/20	1/20	1/20	No NAB
AAV2/2	1/640	1/1280	1/5120	No NAB
AAV2/5	No NAB	1/40	1/160	No NAB
AAV2/7	1/81920	1/81920	1/40960	1/640
AAV2/8	1/640	1/640	1/320	1/5120
<b>Ch.5</b> AAV2/A3	1/20	1/160	1/640	1/640
<b>rh.8</b> AAV2/43.25	1/20	1/20	1/20	1/320
<b>rh.10</b> AAV2/44.2	No NAB	No NAB	No NAB	1/5120
<b>rh.13</b> AAV2/42.2	1/5120	1/5120	1/5120	No NAB
<b>rh.21</b> AA V2/42.10	1/5120	1/10240	1/5120	1/20
<b>rh.22</b> AAV2/42.11	1/20480	1/20480	1/40960	No NAB
<b>rh.24</b> AAV2/42.13	No NAB	1/20	1/20	1/5120

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Table 11b. Cross-NAB assay in 8431 cells and Adv coinfection Infection in 8431 cells (coinfecting with Adv) with:

Serum from rabbit immunized with:	10 <sup>9</sup> GC	10 <sup>10</sup> GC	10 <sup>10</sup> GC	10 <sup>9</sup> GC	10 <sup>9</sup> GC
	<b>rh.12</b>	<b>ch.5</b>	<b>rh. 8</b>	<b>rh.10</b>	<b>rh.20</b>
	AAV2/42.1B	AAV2/A3	AAV2/43.25	AAV2/44.2	AAV2/42.8.2
AAV2/1	No NAB	1/20480	No NAB	1/80	ND
AAV2/2	1/20	No NAB	No NAB	No NAB	ND
AAV2/5	No NAB	1/320	No NAB	No NAB	ND
AAV2/7	1/2560	1/640	1/160	1/81920	ND
AAV2/8	1/10240	1/2560	1/2560	1/81920	ND
<b>ch.5</b> AAV2/A3	1/1280	1/10240	ND	1/5120	1/320
<b>rh.8</b> AAV2/43.25	1/1280	ND	1/20400	1/5120	1/2560
<b>rh.10</b> AAV2/44.2	1/5120	ND	ND	1/5120	1/5120
<b>rh.13</b> AAV2/42.2	1/20	ND	ND	No NAB	1/320
<b>rh.21</b> AAV2/42.10	1/20	ND	ND	1/40	1/80
<b>rh.22</b> AAV2/42.1 1	No NAB	ND	ND	ND	No NAB
<b>rh.24</b> AAV2/42.13	1/5120	ND	ND	ND	1/2560

Table 12

Titer of rabbit sera			Titer after Boosting
Vector		Titer d21	
<b>ch.5</b>	AAV2/A3	1/10,240	1/40,960
<b>rh.8</b>	AAV2/43.25	1/20,400	1/163,840
<b>rh.10</b>	AAV2/44.2	1/10,240	1/527,680
<b>rh.13</b>	AAV2/42.2	1/5,120	1/20,960
<b>rh.21</b>	AAV2/42.10	1/20,400	1/81,920
<b>rh.22</b>	AAV2/42.11	1/40,960	N D
<b>rh.24</b>	AAV2/42.13	1/5,120	ND

Table 13 a. Infection in 8431 cells (coinfecting with Adv) with GFP

	10 <sup>9</sup> GC/well	10 <sup>9</sup> GC/well	10 <sup>9</sup> GC/well	10 <sup>9</sup> GC/well	10 <sup>9</sup> GC/well	10 <sup>9</sup> GC/well
						<b>ch.5</b>
	AAV2/1	AAV2/2	AAV2/5	AAV2/7	AAV2/8	AAV2/A3
# GFU/field	128	>200	95	56	13	1
	83	>200	65	54	11	1

	10 <sup>9</sup> GC/well	10 <sup>9</sup> GC/well	10 <sup>9</sup> GC/well	10 <sup>9</sup> GC/well	10 <sup>9</sup> GC/well	10 <sup>9</sup> GC/well	10 <sup>9</sup> GC/well
	<i>rh.8</i>	<i>rh.10</i>	<i>rh.13</i>	<i>rh.21</i>	<i>rh.22</i>	<i>rh.24</i>	<i>rh.12</i>
	AAV2/43.25	AAV2/44.2	AAV2/42.2	AAV2/42.10	AAV2/42.11	AAV2/42.13	AAV2/42.1B
# GFU/field	3	13	54	62	10	3	18
	2	12	71	60	14	2	20
			48	47	16	3	12

## Example 10 - Mouse Model of Familial Hypercholesterolemia

**[0124]** The following experiment demonstrates that the AAV2/7 construct of the invention delivers the LDL receptor and express LDL receptor in an amount sufficient to reduce the levels of plasma cholesterol and triglycerides in animal models of familial hypercholesterolemia.

## A. Vector Construction

**[0125]** AAV vectors packaged with AAV7 or AAV8 capsid proteins were constructed using a pseudotyping strategy [Hildinger M, *et al.*, *J. Virol* 2001; 75:6199-6203]. Recombinant AAV genomes with AAV2 inverted terminal repeats (ITR) were packaged by triple transfection of 293 cells with the *cis*-plasmid, the adenovirus helper plasmid and a chimeric packaging construct, a fusion of the capsids of the novel AAV serotypes with the rep gene of AAV2. The chimeric packaging plasmid was constructed as previously described [Hildinger et al, cited above]. The recombinant vectors were purified by the standard CsCl<sub>2</sub> sedimentation method. To determine the yield TaqMan (Applied Biosystems) analysis was performed using probes and primers targeting the SV40 poly(A) region of the vectors [Gao GP, *et al.*, *Hum Gene Ther.* 2000 Oct 10;11(15):2079-91]. The resulting vectors express the transgene under the control of the human thyroid hormone binding globulin gene promoter (TBG).

## B. Animals

**[0126]** LDL receptor deficient mice on the C57Bl/6 background were purchased from the Jackson Laboratory (Bar Harbor, ME, USA) and maintained as a breeding colony. Mice were given unrestricted access to water and obtained a high fat Western Diet (high % cholesterol) starting three weeks prior vector injection. At day -7 as well at day 0, blood was obtained via retroorbital bleeds and the lipid profile evaluated. The mice were randomly divided into seven groups. The vector was injected via an intraportal injection as previously described ([Chen SJ *et al.*, *Mol Therapy* 2000; 2(3), 256-261]. Briefly, the mice were anaesthetized with ketamine and xylazine. A laparotomy was performed and the portal vein exposed. Using a 30g needle the appropriate dose of vector diluted in 100ul PBS was directly injected into the portal vein. Pressure was applied to the injection site to ensure a stop of the bleeding. The skin wound was closed and draped and the mice carefully monitored for the following day. Weekly bleeds were performed starting at day 14 after liver directed gene transfer to measure blood lipids. Two animals of each group were sacrificed at the time points week 6 and week 12 after vector injection to examine atherosclerotic plaque size as well as receptor expression. The remaining mice were sacrificed at week 20 for plaque measurement and determination of transgene expression.

Table 14

	Vector	dose	n
Group 1	AAV2/7-TBG-hLDLr	1x 10 <sup>12</sup> gc	12
Group 2	AAV2/7-TBG-hLDLr	3x 10 <sup>11</sup> gc	12
Group 3	AAV2/7-TBG-hLDLr	1x 10 <sup>11</sup> gc	12
Group 4	AAV2/8-TBG-hLDLr	1x 10 <sup>12</sup> gc	12
Group 5	AAV2/8-TBG-hLDLr	3x 10 <sup>11</sup> gc	12
Group 6	AAV2/8-TBG-hLDLr	1x 10 <sup>11</sup> gc	12
Group 7	AAV2/7-TBG-LacZ	1x 10 <sup>11</sup> gc	16

## C. Serum lipoprotein and liver function analysis

**[0127]** Blood samples were obtained from the retroorbital plexus after a 6 hour fasting period. The serum was separated from the plasma by centrifugation. The amount of plasma lipoproteins and liver transaminases in the serum were detected using an automatized clinical chemistry analyzer (ACE, Schiapparelli Biosystems, Alpha Wassermann)

## D. Detection of transgene expression

**[0128]** LDL receptor expression was evaluated by immuno-fluorescence staining and Western blotting. For Western Blot frozen liver tissue was homogenized with lysis buffer (20 mM Tris, pH7.4, 130mM NaCl, 1% Triton X 100, proteinase inhibitor (complete, EDTA-free, Roche, Mannheim, Germany). Protein concentration was determined using the Micro

BCA Protein Assay Reagent Kit (Pierce, Rockford, IL). 40 µg of protein was resolved on 4- 15% Tris-HCl Ready Gels (Biorad, Hercules, CA) and transferred to a nitrocellulose membrane (Invitrogen,). To generate Anti-hLDL receptor antibodies a rabbit was injected intravenously with an AdhLDLr prep ( $1 \times 10^{13}$  GC). Four weeks later the rabbit serum was obtained and used for Western Blot. A 1:100 dilution of the serum was used as a primary antibody followed by a HRP-conjugated anti-rabbit IgG and ECL chemiluminescent detection (ECL Western Blot Detection Kit, Amersham, Arlington Heights, IL).

#### E. Immunocytochemistry

**[0129]** For determination of LDL receptor expression in frozen liver sections immunohistochemistry analyses were performed. 10µm cryostat sections were either fixed in acetone for 5 minutes, or unfixed. Blocking was obtained *via* a 1 hour incubation period with 10% of goat serum. Sections were then incubated for one hour with the primary antibody at room temperature. A rabbit polyclonal antibody anti-human LDL (Biomedical Technologies Inc., Stoughton, MA) was used diluted accordingly to the instructions of the manufacturer. The sections were washed with PBS, and incubated with 1:100 diluted fluorescein goat anti-rabbit IgG (Sigma, St Louis, MO). Specimens were finally examined under fluorescence microscope Nikon Microphot-FXA. In all cases, each incubation was followed by extensive washing with PBS. Negative controls consisted of preincubation with PBS, omission of the primary antibody, and substitution of the primary antibody by an isotype-matched non-immune control antibody. The three types of controls mentioned above were performed for each experiment on the same day.

#### F. Gene transfer efficiency

**[0130]** Liver tissue was obtained after sacrificing the mice at the designated time points. The tissue was shock frozen in liquid nitrogen and stored at -80°C until further processing. DNA was extracted from the liver tissue using a QIAamp DNA Mini Kit (QIAGEN GmbH, Germany) according to the manufacturers protocol. Genome copies of AAV vectors in the liver tissue were evaluated using Taqman analysis using probes and primers against the SV40 poly(A) tail as described above.

#### G. Atherosclerotic plaque measurement

**[0131]** For the quantification of the atherosclerotic plaques in the mouse aorta the mice were anaesthetized (10% ketamine and xylazine, ip), the chest opened and the arterial system perfused with ice-cold phosphate buffered saline through the left ventricle. The aorta was then carefully harvested, slit down along the ventral midline from the aortic arch down to the femoral arteries and fixed in formalin. The lipid-rich atherosclerotic plaques were stained with Sudan IV (Sigma, Germany) and the aorta pinned out flat on a black wax surface. The image was captured with a Sony DXC-960 MD color video camera. The area of the plaque as well as of the complete aortic surface was determined using Phase 3 Imaging Systems (Media Cybernetics).

#### H. Clearance of $I^{125}$ LDL

**[0132]** Two animals per experimental group were tested. A bolus of  $I^{125}$ -labeled LDL (generously provided by Dan Rader, U Penn) was infused slowly through the tail vein over a period of 30 sec (1,000,000 counts of [ $I^{125}$ ]-LDL diluted in 100µl sterile PBS/ animal). At time points 3min, 30 min, 1.5hr, 3hr, 6hr after injection a blood sample was obtained *via* the retro-orbital plexus. The plasma was separated off from the whole blood and 10µl plasma counted in the gamma counter. Finally the fractional catabolic rate was calculated from the lipoprotein clearance data.

#### I. Evaluation of Liver Lipid accumulation

**[0133]** Oil Red Staining of frozen liver sections was performed to determine lipid accumulation. The frozen liver sections were briefly rinsed in distilled water followed by a 2 minute incubation in absolute propylene glycol. The sections were then stained in oil red solution (0.5% in propylene glycol) for 16 hours followed by counterstaining with Mayer's hematoxylin solution for 30 seconds and mounting in warmed glycerin jelly solution.

**[0134]** For quantification of the liver cholesterol and triglyceride content liver sections were homogenized and incubated in chloroform/methanol (2:1) overnight. After adding of 0.05%  $H_2SO_4$  and centrifugation for 10 minutes, the lower layer of each sample was collected, divided in two aliquots and dried under nitrogen. For the cholesterol measurement the dried lipids of the first aliquot were dissolved in 1% Triton X-100 in chloroform. Once dissolved, the solution was dried under nitrogen. After dissolving the lipids in  $ddH_2O$  and incubation for 30 minutes at 37 °C the total cholesterol concentration was measured using a Total Cholesterol Kit (Wako Diagnostics). For the second aliquot the dried lipids were dissolved

in alcoholic KOH and incubated at 60°C for 30 minutes. Then 1 M MgCl<sub>2</sub> was added, followed by incubation on ice for 10 minutes and centrifugation at 14,000 rpm for 30 minutes. The supernatant was finally evaluated for triglycerides (Wako Diagnostics).

[0135] All of the vectors pseudotyped in an AAV2/8 or AAV2/7 capsid lowered total cholesterol, LDL and triglycerides as compared to the control. These test vectors also corrected phenotype of hypercholesterolemia in a dose-dependent manner. A reduction in plaque area for the AAV2/8 and AAV2/7 mice was observed in treated mice at the first test (2 months), and the effect was observed to persist over the length of the experiment (6 months).

#### Example 10 - Functional Factor IX Expression and Correction of Hemophilia

##### A. Knock-Out Mice

[0136] Functional canine factor IX (FIX) expression was assessed in hemophilia B mice. Vectors with capsids of AAV1, AAV2, AAV5, AAV7 or AAV8 were constructed to deliver AAV2 5' ITR - liver-specific promoter [LSP] - canine FIX - woodchuck hepatitis post-regulatory element (WPRE) - AAV2 3' ITR. The vectors were constructed as described in Wang et al, 2000, *Molecular Therapy* 2: 154-158), using the appropriate capsids.

[0137] Knock-out mice were generated as described in Wang et al, 1997. *Proc. Natl. Acad. Sci. USA* 94: 11563-11566. This model closely mimics the phenotypes of hemophilia B in human.

[0138] Vectors of different serotypes (AAV1, AAV2, AAV5, AAV7 and AAV8) were delivered as a single intraportal injection into the liver of adult hemophilic C57Bl/6 mice in a dose of  $1 \times 10^{11}$  GC/mouse for the five different serotypes and one group received an AAV8 vector at a lower dose,  $1 \times 10^{10}$  GC/mouse. Control group was injected with  $1 \times 10^{11}$  GC of AAV2/8 TBG LacZ3. Each group contains 5-10 male and female mice. Mice were bled bi-weekly after vector administration.

##### 1. ELISA

[0139] The canine FIX concentration in the mouse plasma was determined by an ELISA assay specific for canine factor IX, performed essentially as described by Axelrod et al, 1990, *Proc. Natl. Acad. Sci. USA*, 87:5173-5177 with modifications. Sheep anti-canine factor IX (Enzyme Research Laboratories) was used as primary antibody and rabbit anti-canine factor IX ((Enzyme Research Laboratories) was used as secondary antibody. Beginning at two weeks following injection, increased plasma levels of cFIX were detected for all test vectors. The increased levels were sustained at therapeutic levels throughout the length of the experiment, i.e., to 12 weeks. Therapeutic levels are considered to be 5% of normal levels, i.e., at about 250 ng/mL.

[0140] The highest levels of expression were observed for the AAV2/8 (at  $10^{11}$ ) and AAV2/7 constructs, with sustained superphysiology levels cFIX levels (ten-fold higher than the normal level). Expression levels for AAV2/8 ( $10^{11}$ ) were approximately 10 fold higher than those observed for AAV2/2 and AAV2/8 ( $10^{10}$ ). The lowest expression levels, although still above the therapeutic range, were observed for AAV2/5.

##### 2. In Vitro Activated Partial Thromboplastin time (aPTT) Assay

[0141] Functional factor IX activity in plasma of the FIX knock-out mice was determined by an *in vitro* activated partial thromboplastin time (aPTT) assay-Mouse blood samples were collected from the retro-orbital plexus into 1/10 volume of citrate buffer. The aPTT assay was performed as described by Wang et al, 1997, *Proc. Natl. Acad. Sci. USA* 94: 11563-11566.

[0142] Clotting times by aPTT on plasma samples of all vector injected mice were within the normal range (approximately 60 sec) when measured at two weeks post-injection, and sustained clotting times in the normal or shorter than normal range throughout the study period (12 weeks).

[0143] Lowest sustained clotting times were observed in the animals receiving AAV2/8 ( $10^{11}$ ) and AAV2/7. By week 12, AAV2/2 also induced clotting times similar to those for AAV2/8 and AAV2/7. However, this lowered clotting time was not observed for AAV2/2 until week 12, whereas lowered clotting times (in the 25 - 40 sec range) were observed for AAV2/8 and AAV2/7 beginning at week two.

[0144] Immuno-histochemistry staining on the liver tissues harvested from some of the treated mice is currently being performed. About 70-80% of hepatocytes are stained positive for canine FIX in the mouse injected with AAV2/8.cFIX vector.

##### B. Hemophilia B Dogs

[0145] Dogs that have a point mutation in the catalytic domain of the F.IX gene, which, based on modeling studies,

appears to render the protein unstable, suffer from hemophilia B [Evans et al, 1989, Proc. Natl. Acad. Sci. USA, 86:10095-10099]. A colony of such dogs has been maintained for more than two decades at the University of North Carolina, Chapel Hill. The homeostatic parameters of these dogs are well described and include the absence of plasma F.IX antigen, whole blood clotting times in excess of 60 minutes, whereas normal dogs are 6-8 minutes, and prolonged activated partial thromboplastin time of 50-80 seconds, whereas normal dogs are 13-28 seconds. These dogs experience recurrent spontaneous hemorrhages. Typically, significant bleeding episodes are successfully managed by the single intravenous infusion of 10 ml/kg of normal canine plasma; occasionally, repeat infusions are required to control bleeding.

**[0146]** Four dogs are injected intraportally with AAV.cFIX according to the schedule below. A first dog receives a single injection with AAV2/2.cFIX at a dose of  $3.7 \times 10^{11}$  genome copies (GC)/kg. A second dog receives a first injection of AAV2/2.cFIX ( $2.8 \times 10^{11}$  GC/kg), followed by a second injection with AAV2/7.cFIX ( $2.3 \times 10^{13}$  GC/kg) at day 1180. A third dog receives a single injection with AAV2/2.cFIX at a dose of  $4.6 \times 10^{12}$  GC/kg. The fourth dog receives an injection with AAV2/2.cFIX ( $2.8 \times 10^{12}$  GC/kg) and an injection at day 99.5 with AAV2/7.cFIX ( $5 \times 10^{12}$  GC/kg).

**[0147]** The abdomen of hemophilia dogs are aseptically and surgically opened under general anesthesia and a single infusion of vector is administered into the portal vein. The animals are protected from hemorrhage in the peri-operative period by intravenous administration of normal canine plasma. The dog is sedated, intubated to induce general anesthesia, and the abdomen shaved and prepped. After the abdomen is opened, the spleen is moved into the operative field. The splenic vein is located and a suture is loosely placed proximal to a small distal incision in the vein. A needle is rapidly inserted into the vein, then the suture loosened and a 5 F cannula is threaded to an intravenous location near the portal vein threaded to an intravenous location near the portal vein bifurcation. After hemostasis is secured and the catheter balloon inflated, approximately 5.0 ml of vector diluted in PBS is infused into the portal vein over a 5 minute interval. The vector infusion is followed by a 5.0 ml infusion of saline. The balloon is then deflated, the cannula removed and venous hemostasis is secured. The spleen is then replaced, bleeding vessels are cauterized and the operative wound is closed. The animal is extubated having tolerated the surgical procedure well. Blood samples are analyzed as described. [Wang et al, 2000, *Molecular Therapy* 2: 154-158]

**[0148]** Results showing correction or partial correction are anticipated for AAV2/7.

#### SEQUENCE LISTING

##### **[0149]**

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<120> A Method of Detecting and/or Identifying Adeno-Associated Virus (AAV) Sequences and Isolating Novel Sequences Identified Thereby

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<213> capsid protein of adeno-associated virus serotype 7

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Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
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Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
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Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
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<211> 623

<212> PRT

<213> rep protein of adeno-associated virus serotype 7

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 Asn Gly Tyr Asp Pro Ala Tyr Ala Gly Ser Val Phe Leu Gly Trp Ala  
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 Gln Lys Lys Phe Gly Lys Arg Asn Thr Ile Trp Leu Phe Gly Pro Ala  
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 Thr Thr Gly Lys Thr Asn Ile Ala Glu Ala Ile Ala His Ala Val Pro  
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 Phe Tyr Gly Cys Val Asn Trp Thr Asn Glu Asn Phe Pro Phe Asn Asp  
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 Cys Val Asp Lys Met Val Ile Trp Trp Glu Glu Gly Lys Met Thr Ala  
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# EP 1 310 571 B1

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EP 1 310 571 B1

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EP 1 310 571 B1

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# EP 1 310 571 B1

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<212> DNA

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EP 1 310 571 B1

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EP 1 310 571 B1

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## EP 1 310 571 B1

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EP 1 310 571 B1

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<212> DNA

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<400> 27

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<210> 28

<211> 3128

<212> DNA

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<213> new AAV serotype, clone 42.15

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<211> 3197

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<213> new AAV serotype, clone 42.3a

<400> 32

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<212> DNA

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<400> 33

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# EP 1 310 571 B1

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EP 1 310 571 B1

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# EP 1 310 571 B1

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<210> 36

<211> 2495

<212> DNA

15 <213> new AAV serotype, clone 42.3b

<400> 36

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EP 1 310 571 B1

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# EP 1 310 571 B1

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EP 1 310 571 B1

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EP 1 310 571 B1

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# EP 1 310 571 B1

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EP 1 310 571 B1

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EP 1 310 571 B1

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<213> new AAV serotype, clone 43.20

<400> 42

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<210> 44  
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<400> 44

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<211> 3128

<212> DNA

<213> new AAV serotype, clone 44.1

<400> 46

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<210> 47

<211> 3128

40 <212> DNA

<213> new AAV serotype, clone 44.5

<400> 47

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# EP 1 310 571 B1

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	<211> 1933
	<212> DNA
	<213> new AAV serotype, clone 223.10
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	<222> (1302)..(1302)
	<223> can be a, c, g or t
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# EP 1 310 571 B1

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# EP 1 310 571 B1

5  
 10  
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<210> 49

<211> 1933

<212> DNA

<213> new AAV serotype, clone 223.2

<400> 49



# EP 1 310 571 B1

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	taagacggca cctggaaaga agcgaccggt agactcgcca gactccacct cgggcatcgg	240
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	agtgggtaat gcctcaggaa attggcattg cgattccaca tggctgggcg acagagtcac	480
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# EP 1 310 571 B1

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<210> 50

<211> 1933

<212> DNA

<213> new AAV serotype, clone 223.4

<400> 50

EP 1 310 571 B1

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**EP 1 310 571 B1**

<210> 51

<211> 1933

<212> DNA

<213> new AAV serotype, clone 223.5

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<400> 51

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EP 1 310 571 B1

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# EP 1 310 571 B1

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<212> DNA

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EP 1 310 571 B1

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EP 1 310 571 B1

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# EP 1 310 571 B1

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<400> 60

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10 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
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Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
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 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
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 Lys Gly Lys Gln Pro Ala Lys Lys Arg Leu Asn Phe Glu Glu Asp Thr  
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 Ser Asp Ile Glu Met Arg Ala Ala Pro Gly Gly Asn Ala Val Asp Ala  
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 260 265 270  
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Cys Gly Ile Val Thr Gly Glu Asn Gln Asn Gln Thr Asp Arg Asn Ala  
370 375 380

15 Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met Leu Arg Thr Gly Asn  
385 390 395 400

20 Asn Phe Glu Met Ala Tyr Asn Phe Gly Lys Val Pro Phe His Ser Met  
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Gln Gly Asn Ala Ala Thr Thr Phe Gly Lys Ile Arg Ser Gly Asp Phe  
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50 Thr Gly Asn Thr Thr Thr Ser Ala Asn Asn Leu Leu Phe Thr Ser Glu  
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Glu Glu Ile Ala Ala Thr Asn Pro Arg Asp Thr Asp Met Phe Gly Gln  
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Val Thr Ala Met Gly Val Leu Pro Gly Met Val Trp Gln Asn Arg Asp  
595 600 605

Ile Tyr Tyr Gln Gly Pro Ile Trp Ala Lys Ile Pro His Ala Asp Gly  
610 615 620

His Phe His Pro Ser Pro Leu Ile Gly Gly Phe Gly Leu Lys His Pro  
625 630 635 640

Pro Pro Gln Ile Phe Ile Lys Asn Thr Pro Val Pro Ala Asn Pro Ala  
645 650 655

Thr Thr Phe Thr Ala Ala Arg Val Asp Ser Phe Ile Thr Gln Tyr Ser  
660 665 670

Thr Gly Gln Val Ala Val Gln Ile Glu Trp Glu Ile Glu Lys Glu Arg  
675 680 685

Ser Lys Arg Trp Asn Pro Glu Val Gln Phe Thr Ser Asn Tyr Gly Asn  
690 695 700

Gln Ser Ser Met Leu Trp Ala Pro Asp Thr Thr Gly Lys Tyr Thr Glu  
705 710 715 720

Pro Arg Val Ile Gly Ser Arg Tyr Leu Thr Asn His Leu  
725 730

<210> 61

<211> 733

<212> PRT

<213> capsid protein of AAV serotype, clone C2VP1

<400> 61

EP 1 310 571 B1

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
1 5 10 15

5 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Leu  
20 25 30

10 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe His Gly Leu Asp Lys Gly Glu Pro  
50 55 60

15 Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

20

25

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EP 1 310 571 B1

5  
 10  
 15  
 20  
 25  
 30  
 35  
 40  
 45  
 50  
 55

Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
 85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
 100 105 110

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
 115 120 125

Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
 130 135 140

Pro Leu Glu Ser Pro Gln Glu Pro Asp Ser Ser Ser Gly Ile Gly Lys  
 145 150 155 160

Lys Gly Lys Gln Pro Ala Lys Lys Arg Leu Asn Phe Glu Glu Asp Thr  
 165 170 175

Gly Ala Gly Asp Gly Pro Pro Glu Gly Ser Asp Thr Ser Ala Met Ser  
 180 185 190

Ser Asp Ile Glu Met Arg Ala Ala Pro Gly Gly Asn Ala Val Asp Ala  
 195 200 205

Gly Gln Gly Ser Asp Gly Val Gly Asn Ala Ser Gly Asp Trp His Cys  
 210 215 220

Asp Ser Thr Trp Ser Glu Gly Lys Val Thr Thr Thr Ser Thr Arg Thr  
 225 230 235 240

Trp Val Leu Pro Thr Tyr Asn Asn His Leu Tyr Leu Arg Leu Gly Thr  
 245 250 255

Thr Ser Asn Ser Asn Thr Tyr Asn Gly Phe Ser Thr Pro Trp Gly Tyr  
 260 265 270

Phe Asp Phe Asn Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln  
 275 280 285

Arg Leu Ile Asn Asn Asn Trp Gly Leu Arg Pro Lys Ala Met Arg Val  
 290 295 300

Lys Ile Phe Asn Ile Gln Val Lys Glu Val Thr Thr Ser Asn Gly Glu  
 305 310 315 320

Thr Thr Val Ala Asn Asn Leu Thr Ser Thr Val Gln Ile Phe Ala Asp  
 325 330 335

EP 1 310 571 B1

Ser Ser Tyr Glu Leu Pro Tyr Val Met Asp Ala Gly Gln Glu Gly Ser  
 340 345 350  
 5  
 Leu Pro Pro Phe Pro Asn Asp Val Phe Met Val Pro Gln Tyr Gly Tyr  
 355 360 365  
 10  
 Cys Gly Ile Val Thr Gly Glu Asn Gln Asn Gln Thr Asp Arg Asn Ala  
 370 375 380  
 Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met Leu Arg Thr Gly Asn  
 385 390 395 400  
 15  
 Asn Phe Glu Met Ala Tyr Asn Phe Glu Lys Val Pro Phe His Ser Met  
 405 410 415  
 Tyr Ala His Ser Gln Ser Leu Asp Arg Leu Met Asn Pro Leu Leu Asp  
 420 425 430  
 20  
 Gln Tyr Leu Trp His Leu Gln Ser Thr Thr Ser Gly Glu Thr Leu Asn  
 435 440 445  
 25  
 Gln Gly Asn Ala Ala Thr Thr Phe Gly Lys Ile Arg Ser Gly Asp Phe  
 450 455 460  
 Ala Phe Tyr Arg Lys Asn Trp Leu Pro Gly Pro Cys Val Lys Gln Gln  
 465 470 475 480  
 30  
 Arg Phe Ser Lys Thr Ala Ser Gln Asn Tyr Lys Ile Pro Ala Ser Gly  
 485 490 495  
 35  
 Gly Asn Ala Leu Leu Lys Tyr Asp Thr His Tyr Thr Leu Asn Asn Arg  
 500 505 510  
 Trp Ser Asn Ile Ala Pro Gly Pro Pro Met Ala Thr Ala Gly Pro Ser  
 515 520 525  
 40  
 Asp Gly Asp Phe Ser Asn Ala Gln Leu Ile Phe Pro Gly Pro Ser Val  
 530 535 540  
 45  
 Thr Gly Asn Thr Thr Thr Ser Ala Asn Asn Leu Leu Phe Thr Ser Glu  
 545 550 555 560  
 Gly Glu Ile Ala Ala Thr Asn Pro Arg Asp Thr Asp Met Phe Gly Gln  
 565 570 575  
 50  
 Ile Ala Asp Asn Asn Gln Asn Ala Thr Thr Ala Pro Ile Thr Gly Asn  
 580 585 590  
 55

# EP 1 310 571 B1

Val Thr Ala Met Gly Val Leu Pro Gly Met Val Trp Gln Asn Arg Asp  
 595 600 605  
 5  
 Ile Tyr Tyr Gln Gly Pro Ile Trp Ala Lys Ile Pro His Ala Asp Gly  
 610 615 620  
 10  
 His Phe His Pro Ser Pro Leu Ile Gly Gly Phe Gly Leu Lys His Pro  
 625 630 635 640  
 Pro Pro Gln Ile Phe Ile Lys Asn Thr Pro Val Pro Ala Asn Pro Ala  
 645 650 655  
 15  
 Thr Thr Phe Thr Ala Ala Arg Val Asp Ser Phe Ile Thr Gln Tyr Ser  
 660 665 670  
 Thr Gly Gln Val Ala Val Gln Ile Glu Trp Glu Ile Glu Lys Glu Arg  
 675 680 685  
 20  
 Ser Lys Arg Arg Asn Pro Glu Val Gln Phe Thr Ser Asn Tyr Gly Asn  
 690 695 700  
 25  
 Gln Ser Ser Met Leu Trp Ala Pro Asp Thr Thr Gly Lys Tyr Thr Glu  
 705 710 715 720  
 Pro Arg Val Ile Gly Ser Arg Tyr Leu Thr Asn His Leu  
 725 730  
 30

<210> 62

<211> 733

35 <212> PRT

<213> capsid protein of AAV serotype, clone C5VP1@2

<400> 62

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EP 1 310 571 B1

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
1 5 10 15

5 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
20 25 30

10 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
35 40 45

Gly Tyr Glu Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60

15 Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

20 Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
85 90 95

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EP 1 310 571 B1

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
 100 105 110  
 5  
 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
 115 120 125  
 10  
 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
 130 135 140  
 Pro Leu Glu Ser Pro Gln Glu Pro Asp Ser Ser Ser Gly Ile Gly Lys  
 145 150 155 160  
 15  
 Lys Gly Lys Gln Pro Ala Lys Lys Arg Leu Asn Phe Glu Glu Asp Thr  
 165 170 175  
 20  
 Gly Ala Gly Asp Gly Pro Pro Glu Gly Ser Asp Thr Ser Ala Met Ser  
 180 185 190  
 Ser Asp Ile Glu Met Arg Ala Ala Pro Gly Gly Asn Ala Val Asp Ala  
 195 200 205  
 25  
 Gly Gln Gly Ser Asp Gly Val Gly Asn Ala Ser Gly Asp Trp His Cys  
 210 215 220  
 30  
 Asp Ser Thr Trp Ser Glu Gly Lys Val Thr Thr Thr Ser Thr Arg Thr  
 225 230 235 240  
 Trp Val Leu Pro Thr Tyr Asn Asn His Leu Tyr Leu Arg Leu Gly Thr  
 245 250 255  
 35  
 Thr Ser Asn Ser Asn Thr Tyr Asn Gly Phe Ser Thr Pro Trp Gly Tyr  
 260 265 270  
 40  
 Phe Asp Phe Asn Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln  
 275 280 285  
 Arg Leu Ile Asn Asn Asn Trp Gly Leu Arg Pro Lys Ala Met Arg Val  
 290 295 300  
 45  
 Lys Ile Phe Asn Ile Gln Val Lys Glu Val Thr Thr Ser Asn Gly Glu  
 305 310 315 320  
 50  
 Thr Thr Val Ala Asn Asn Leu Thr Ser Thr Val Gln Ile Phe Ala Asp  
 325 330 335  
 Ser Ser Tyr Glu Leu Pro Tyr Val Met Asp Ala Gly Gln Glu Gly Ser  
 340 345 350  
 55



EP 1 310 571 B1

Leu Pro Pro Phe Pro Asn Asp Val Phe Met Val Pro Gln Tyr Gly Tyr  
355 360 365

5 Cys Gly Ile Val Thr Gly Glu Asn Gln Asn Gln Thr Asp Arg Asn Ala  
370 375 380

10 Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met Leu Arg Thr Gly Asn  
385 390 395 400

Asn Phe Glu Thr Ala Tyr Asn Phe Glu Lys Val Pro Phe His Ser Met  
405 410 415

15 Tyr Ala His Ser Gln Ser Leu Asp Gly Leu Met Asn Pro Leu Leu Asp  
420 425 430

20 Gln Tyr Leu Trp His Leu Gln Ser Thr Thr Ser Gly Glu Thr Leu Asn  
435 440 445

Gln Gly Asn Ala Ala Thr Thr Phe Gly Lys Ile Arg Ser Gly Asp Phe  
450 455 460

25 Ala Phe Tyr Arg Lys Asn Trp Leu Pro Gly Pro Cys Val Lys Gln Gln  
465 470 475 480

30 Arg Phe Ser Lys Thr Ala Ser Gln Asn Tyr Lys Ile Pro Ala Ser Gly  
485 490 495

Gly Asn Ala Leu Leu Lys Tyr Asp Thr His Tyr Thr Leu Asn Asn Arg  
500 505 510

35 Trp Ser Asn Ile Ala Pro Gly Pro Pro Met Ala Thr Ala Gly Pro Ser  
515 520 525

40 Asp Gly Asp Phe Ser Asn Ala Gln Leu Ile Phe Pro Gly Pro Ser Val  
530 535 540

Thr Gly Asn Thr Thr Thr Ser Ala Asn Asn Leu Leu Phe Thr Ser Glu  
545 550 555 560

45 Glu Glu Ile Ala Ala Thr Asn Pro Arg Asp Thr Asp Met Phe Gly Gln  
565 570 575

50 Ile Ala Asp Asn Asn Gln Asn Ala Thr Thr Ala Pro Ile Thr Gly Asn  
580 585 590

Val Thr Ala Met Gly Val Leu Pro Gly Met Val Trp Gln Asn Arg Asp  
595 600 605

# EP 1 310 571 B1

	Ile	Tyr	Tyr	Gln	Gly	Pro	Ile	Trp	Ala	Lys	Ile	Pro	His	Ala	Asp	Gly
	610						615					620				
5	His	Phe	His	Pro	Ser	Pro	Leu	Ile	Gly	Gly	Phe	Gly	Leu	Lys	His	Pro
	625					630					635					640
	Pro	Pro	Gln	Ile	Phe	Ile	Lys	Asn	Thr	Pro	Val	Pro	Ala	Tyr	Pro	Ala
10					645					650					655	
	Thr	Thr	Phe	Thr	Ala	Ala	Arg	Val	Asp	Ser	Phe	Ile	Thr	Gln	Tyr	Ser
				660					665					670		
15	Thr	Gly	Gln	Val	Ala	Val	Gln	Ile	Glu	Trp	Glu	Ile	Glu	Lys	Glu	Arg
			675					680					685			
	Ser	Lys	Arg	Trp	Asn	Pro	Glu	Val	Gln	Phe	Thr	Ser	Asn	Cys	Gly	Asn
20		690					695					700				
	Gln	Ser	Ser	Met	Leu	Trp	Ala	Pro	Asp	Thr	Thr	Gly	Lys	Tyr	Thr	Glu
	705					710					715					720
25	Pro	Arg	Val	Ile	Gly	Ser	Arg	Tyr	Leu	Thr	Asn	His	Leu			
					725					730						

<210> 63

30 <211> 734

<212> PRT

<213> capsid protein of AAV serotype, clone AAV4VP1

<400> 63

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EP 1 310 571 B1

Met Thr Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser Glu  
1 5 10 15

5 Gly Val Arg Glu Trp Trp Ala Leu Gln Pro Gly Ala Pro Lys Pro Lys  
20 25 30

10 Ala Asn Gln Gln His Gln Asp Asn Ala Arg Gly Leu Val Leu Pro Gly  
35 40 45

Tyr Lys Tyr Leu Gly Pro Gly Asn Gly Leu Asp Lys Gly Glu Pro Val  
50 55 60

15 Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp Gln  
65 70 75 80

20 Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala Asp  
85 90 95

Ala Glu Phe Gln Gln Arg Leu Gln Gly Asp Thr Ser Phe Gly Gly Asn  
100 105 110

25

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EP 1 310 571 B1

Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro Leu  
 115 120 125  
 5  
 Gly Leu Val Glu Gln Ala Gly Glu Thr Ala Pro Gly Lys Lys Arg Pro  
 130 135 140  
 10  
 Leu Ile Glu Ser Pro Gln Gln Pro Asp Ser Ser Thr Gly Ile Gly Lys  
 145 150 155 160  
 Lys Gly Lys Gln Pro Ala Lys Lys Lys Leu Val Phe Glu Asp Glu Thr  
 165 170 175  
 15  
 Gly Ala Gly Asp Gly Pro Pro Glu Gly Ser Thr Ser Gly Ala Met Ser  
 180 185 190  
 20  
 Asp Asp Ser Glu Met Arg Ala Ala Ala Gly Gly Ala Ala Val Glu Gly  
 195 200 205  
 Gly Gln Gly Ala Asp Gly Val Gly Asn Ala Ser Gly Asp Trp His Cys  
 210 215 220  
 25  
 Asp Ser Thr Trp Ser Glu Gly His Val Thr Thr Thr Ser Thr Arg Thr  
 225 230 235 240  
 30  
 Trp Val Leu Pro Thr Tyr Asn Asn His Leu Tyr Lys Arg Leu Gly Glu  
 245 250 255  
 Ser Leu Gln Ser Asn Thr Tyr Asn Gly Phe Ser Thr Pro Trp Gly Tyr  
 260 265 270  
 35  
 Phe Asp Phe Asn Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln  
 275 280 285  
 40  
 Arg Leu Ile Asn Asn Asn Trp Gly Met Arg Pro Lys Ala Met Arg Val  
 290 295 300  
 Lys Ile Phe Asn Ile Gln Val Lys Glu Val Thr Thr Ser Asn Gly Glu  
 305 310 315 320  
 45  
 Thr Thr Val Ala Asn Asn Leu Thr Ser Thr Val Gln Ile Phe Ala Asp  
 325 330 335  
 50  
 Ser Ser Tyr Glu Leu Pro Tyr Val Met Asp Ala Gly Gln Glu Gly Ser  
 340 345 350  
 55  
 Leu Pro Pro Phe Pro Asn Asp Val Phe Met Val Pro Gln Tyr Gly Tyr  
 355 360 365

EP 1 310 571 B1

Cys Gly Leu Val Thr Gly Asn Thr Ser Gln Gln Gln Thr Asp Arg Asn  
 370 375 380  
 5  
 Ala Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met Leu Arg Thr Gly  
 385 390 395 400  
 10  
 Asn Asn Phe Glu Ile Thr Tyr Ser Phe Glu Lys Val Pro Phe His Ser  
 405 410 415  
 Met Tyr Ala His Ser Gln Ser Leu Asp Arg Leu Met Asn Pro Leu Ile  
 420 425 430  
 15  
 Asp Gln Tyr Leu Trp Gly Leu Gln Ser Thr Thr Thr Gly Thr Thr Leu  
 435 440 445  
 20  
 Asn Ala Gly Thr Ala Thr Thr Asn Phe Thr Lys Leu Arg Pro Thr Asn  
 450 455 460  
 Phe Ser Asn Phe Lys Lys Asn Trp Leu Pro Gly Pro Ser Ile Lys Gln  
 465 470 475 480  
 25  
 Gln Gly Phe Ser Lys Thr Ala Asn Gln Asn Tyr Lys Ile Pro Ala Thr  
 485 490 495  
 30  
 Gly Ser Asp Ser Leu Ile Lys Tyr Glu Thr His Ser Thr Leu Asp Gly  
 500 505 510  
 Arg Trp Ser Ala Leu Thr Pro Gly Pro Pro Met Ala Thr Ala Gly Pro  
 515 520 525  
 35  
 Ala Asp Ser Lys Phe Ser Asn Ser Gln Leu Ile Phe Ala Gly Pro Lys  
 530 535 540  
 40  
 Gln Asn Gly Asn Thr Ala Thr Val Pro Gly Thr Leu Ile Phe Thr Ser  
 545 550 555 560  
 Glu Glu Glu Leu Ala Ala Thr Asn Ala Thr Asp Thr Asp Met Trp Gly  
 565 570 575  
 45  
 Asn Leu Pro Gly Gly Asp Gln Ser Asn Ser Asn Leu Pro Thr Val Asp  
 580 585 590  
 50  
 Arg Leu Thr Ala Leu Gly Ala Val Pro Gly Met Val Trp Gln Asn Arg  
 595 600 605  
 Asp Ile Tyr Tyr Gln Gly Pro Ile Trp Ala Lys Ile Pro His Thr Asp  
 610 615 620  
 55

# EP 1 310 571 B1

Gly His Phe His Pro Ser Pro Leu Ile Gly Gly Phe Gly Leu Lys His  
 625 630 635 640  
 5  
 Pro Pro Pro Gln Ile Phe Ile Lys Asn Thr Pro Val Pro Ala Asn Pro  
 645 650 655  
 10  
 Ala Thr Thr Phe Ser Ser Thr Pro Val Asn Ser Phe Ile Thr Gln Tyr  
 660 665 670  
 Ser Thr Gly Gln Val Ser Val Gln Ile Asp Trp Glu Ile Gln Lys Glu  
 675 680 685  
 15  
 Arg Ser Lys Arg Trp Asn Pro Glu Val Gln Phe Thr Ser Asn Tyr Gly  
 690 695 700  
 20  
 Gln Gln Asn Ser Leu Leu Trp Ala Pro Asp Ala Ala Gly Lys Tyr Thr  
 705 710 715 720  
 Glu Pro Arg Ala Ile Gly Thr Arg Tyr Leu Thr His His Leu  
 725 730  
 25  
 <210> 64  
 <211> 736  
 <212> PRT  
 <213> capsid protein of AAV serotype, clone AAV1  
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 <400> 64  
 35  
 Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
 1 5 10 15  
 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
 20 25 30  
 40  
 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
 35 40 45  
 Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
 50 55 60  
 45  
 Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
 65 70 75 80  
 50  
 Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
 85 90 95  
 Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
 100 105 110  
 55  
 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
 115 120 125

EP 1 310 571 B1

5 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
 130 135 140  
 Pro Val Glu Gln Ser Pro Gln Glu Pro Asp Ser Ser Ser Gly Ile Gly  
 145 150 155 160  
 10 Lys Thr Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln Thr  
 165 170 175  
 Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro Pro  
 180 185 190  
 15 Ala Thr Pro Ala Ala Val Gly Pro Thr Thr Met Ala Ser Gly Gly Gly  
 195 200 205  
 20 Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala  
 210 215 220  
 Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile  
 225 230 235 240  
 25 Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu  
 245 250 255  
 30 Tyr Lys Gln Ile Ser Ser Ala Ser Thr Gly Ala Ser Asn Asp Asn His  
 260 265 270  
 Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe  
 275 280 285  
 35 His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn  
 290 295 300  
 40 Trp Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn Ile Gln  
 305 310 315 320  
 Val Lys Glu Val Thr Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn  
 325 330 335  
 45 Leu Thr Ser Thr Val Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro  
 340 345 350  
 50 Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala  
 355 360 365  
 Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly  
 370 375 380  
 55

EP 1 310 571 B1

5 Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro  
 385 390 395 400  
 Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Thr Phe Ser Tyr Thr Phe  
 405 410 415  
 10 Glu Glu Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp  
 420 425 430  
 Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Asn Arg  
 435 440 445  
 15 Thr Gln Asn Gln Ser Gly Ser Ala Gln Asn Lys Asp Leu Leu Phe Ser  
 450 455 460  
 Arg Gly Ser Pro Ala Gly Met Ser Val Gln Pro Lys Asn Trp Leu Pro  
 465 470 475 480  
 Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Lys Thr Lys Thr Asp Asn  
 485 490 495  
 25 Asn Asn Ser Asn Phe Thr Trp Thr Gly Ala Ser Lys Tyr Asn Leu Asn  
 500 505 510  
 Gly Arg Glu Ser Ile Ile Asn Pro Gly Thr Ala Met Ala Ser His Lys  
 515 520 525  
 Asp Asp Glu Asp Lys Phe Phe Pro Met Ser Gly Val Met Ile Phe Gly  
 530 535 540  
 35 Lys Glu Ser Ala Gly Ala Ser Asn Thr Ala Leu Asp Asn Val Met Ile  
 545 550 555 560  
 Thr Asp Glu Glu Glu Ile Lys Ala Thr Asn Pro Val Ala Thr Glu Arg  
 565 570 575  
 Phe Gly Thr Val Ala Val Asn Phe Gln Ser Ser Ser Thr Asp Pro Ala  
 580 585 590  
 45 Thr Gly Asp Val His Ala Met Gly Ala Leu Pro Gly Met Val Trp Gln  
 595 600 605  
 Asp Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His  
 610 615 620  
 55 Thr Asp Gly His Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu  
 625 630 635 640



# EP 1 310 571 B1

Lys Asn Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala  
645 650 655

5

Asn Pro Pro Ala Glu Phe Ser Ala Thr Lys Phe Ala Ser Phe Ile Thr  
660 665 670

10

Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln  
675 680 685

Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Val Gln Tyr Thr Ser Asn  
690 695 700

15

Tyr Ala Lys Ser Ala Asn Val Asp Phe Thr Val Asp Asn Asn Gly Leu  
705 710 715 720

20

Tyr Thr Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Pro Leu  
725 730 735

<210> 65

<211> 736

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<212> PRT

<213> capsid protein of AAV serotype, clone AAV6VP1

<400> 65

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EP 1 310 571 B1

	Met	Ala	Ala	Asp	Gly	Tyr	Leu	Pro	Asp	Trp	Leu	Glu	Asp	Asn	Leu	Ser
	1				5					10				15		
5	Glu	Gly	Ile	Arg	Glu	Trp	Trp	Asp	Leu	Lys	Pro	Gly	Ala	Pro	Lys	Pro
				20					25					30		
	Lys	Ala	Asn	Gln	Gln	Lys	Gln	Asp	Asp	Gly	Arg	Gly	Leu	Val	Leu	Pro
			35					40					45			
10	Gly	Tyr	Lys	Tyr	Leu	Gly	Pro	Phe	Asn	Gly	Leu	Asp	Lys	Gly	Glu	Pro
		50					55					60				
15	Val	Asn	Ala	Ala	Asp	Ala	Ala	Ala	Leu	Glu	His	Asp	Lys	Ala	Tyr	Asp
	65					70					75					80
	Gln	Gln	Leu	Lys	Ala	Gly	Asp	Asn	Pro	Tyr	Leu	Arg	Tyr	Asn	His	Ala
					85					90					95	
20	Asp	Ala	Glu	Phe	Gln	Glu	Arg	Leu	Gln	Glu	Asp	Thr	Ser	Phe	Gly	Gly
				100					105					110		
25	Asn	Leu	Gly	Arg	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Val	Leu	Glu	Pro
			115					120					125			
	Phe	Gly	Leu	Val	Glu	Glu	Gly	Ala	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Arg
	130						135					140				

EP 1 310 571 B1

5 Pro Val Glu Gln Ser Pro Gln Glu Pro Asp Ser Ser Ser Gly Ile Gly  
145 150 155 160

Lys Thr Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln Thr  
165 170 175

10 Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro Pro  
180 185 190

Ala Thr Pro Ala Ala Val Gly Pro Thr Thr Met Ala Ser Gly Gly Gly  
195 200 205

15 Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala  
210 215 220

20 Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile  
225 230 235 240

Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu  
245 250 255

25 Tyr Lys Gln Ile Ser Ser Ala Ser Thr Gly Ala Ser Asn Asp Asn His  
260 265 270

30 Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe  
275 280 285

His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn  
290 295 300

35 Trp Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn Ile Gln  
305 310 315 320

40 Val Lys Glu Val Thr Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn  
325 330 335

Leu Thr Ser Thr Val Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro  
340 345 350

45 Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala  
355 360 365

50 Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly  
370 375 380

Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro  
385 390 395 400

55

EP 1 310 571 B1

Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Thr Phe Ser Tyr Thr Phe  
 405 410 415  
 5  
 Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp  
 420 425 430  
 10  
 Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Asn Arg  
 435 440 445  
 Thr Gln Asn Gln Ser Gly Ser Ala Gln Asn Lys Asp Leu Leu Phe Ser  
 450 455 460  
 15  
 Arg Gly Ser Pro Ala Gly Met Ser Val Gln Pro Lys Asn Trp Leu Pro  
 465 470 475 480  
 20  
 Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Lys Thr Lys Thr Asp Asn  
 485 490 495  
 Asn Asn Ser Asn Phe Thr Trp Thr Gly Ala Ser Lys Tyr Asn Leu Asn  
 500 505 510  
 25  
 Gly Arg Glu Ser Ile Ile Asn Pro Gly Thr Ala Met Ala Ser His Lys  
 515 520 525  
 30  
 Asp Asp Lys Asp Lys Phe Phe Pro Met Ser Gly Val Met Ile Phe Gly  
 530 535 540  
 Lys Glu Ser Ala Gly Ala Ser Asn Thr Ala Leu Asp Asn Val Met Ile  
 545 550 555 560  
 35  
 Thr Asp Glu Glu Glu Ile Lys Ala Thr Asn Pro Val Ala Thr Glu Arg  
 565 570 575  
 40  
 Phe Gly Thr Val Ala Val Asn Leu Gln Ser Ser Ser Thr Asp Pro Ala  
 580 585 590  
 Thr Gly Asp Val His Val Met Gly Ala Leu Pro Gly Met Val Trp Gln  
 595 600 605  
 45  
 Asp Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His  
 610 615 620  
 50  
 Thr Asp Gly His Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu  
 625 630 635 640  
 Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala  
 645 650 655

# EP 1 310 571 B1

5 Asn Pro Pro Ala Glu Phe Ser Ala Thr Lys Phe Ala Ser Phe Ile Thr  
 660 665 670  
 Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln  
 675 680 685  
 10 Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Val Gln Tyr Thr Ser Asn  
 690 695 700  
 Tyr Ala Lys Ser Ala Asn Val Asp Phe Thr Val Asp Asn Asn Gly Leu  
 705 710 715 720  
 15 Tyr Thr Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Pro Leu  
 725 730 735  
 20 <210> 66  
 <211> 735  
 <212> PRT  
 <213> capsid protein of AAV serotype, clone A3.3  
 25 <400> 66  
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 50  
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EP 1 310 571 B1

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Thr Leu Ser  
1 5 10 15

5 Glu Gly Ile Arg Gln Trp Trp Lys Leu Lys Pro Gly Pro Pro Pro Pro  
20 25 30

10 Lys Pro Asn Gln Gln His Arg Asp Asp Ser Arg Gly Leu Val Leu Pro  
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60

15 Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

20 His Gln Leu Lys Gln Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala  
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
100 105 110

25 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
115 120 125

30 Leu Gly Leu Val Glu Glu Ala Val Lys Thr Ala Pro Gly Lys Lys Arg  
130 135 140

35

40

45

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EP 1 310 571 B1

5 Pro Ile Glu Gln Ser Pro Ala Glu Pro Asp Ser Ser Ser Gly Ile Gly  
 145 150 155 160  
 Lys Ser Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln Thr  
 165 170 175  
 10 Gly Asp Thr Glu Ser Val Pro Gly Pro Gln Pro Ile Gly Glu Pro Pro  
 180 185 190  
 Ala Ala Pro Ser Gly Val Gly Ser Asn Thr Met Ala Ser Gly Gly Gly  
 195 200 205  
 15 Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ser  
 210 215 220  
 20 Ser Gly Asn Trp His Cys Asp Ser Thr Trp Met Gly Asp Arg Val Ile  
 225 230 235 240  
 Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu  
 245 250 255  
 25 Tyr Lys Gln Ile Ser Ser Glu Ser Gly Ala Thr Asn Asp Asn His Tyr  
 260 265 270  
 30 Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His  
 275 280 285  
 Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp  
 290 295 300  
 35 Gly Phe Arg Pro Lys Lys Leu Asn Phe Lys Leu Phe Asn Ile Gln Val  
 305 310 315 320  
 40 Lys Glu Val Thr Gln Asn Asp Gly Thr Thr Thr Ile Ala Asn Asn Leu  
 325 330 335  
 Thr Ser Ala Val Gln Val Phe Thr Asp Ser Glu Tyr Gln Leu Pro Tyr  
 340 345 350  
 45 Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp  
 355 360 365  
 50 Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser  
 370 375 380  
 55 Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser  
 385 390 395 400

EP 1 310 571 B1

5 Gln Met Leu Arg Thr Gly Asn Asn Phe Thr Phe Ser Tyr Thr Phe Glu  
405 410 415

Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg  
420 425 430

10 Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ser Lys Thr  
435 440 445

Gln Gly Thr Ser Gly Thr Thr Gln Gln Ser Arg Leu Gln Phe Ser Gln  
450 455 460

15 Ala Gly Pro Ser Ser Met Ala Gln Gln Ala Lys Asn Trp Leu Pro Gly  
465 470 475 480

20 Pro Ser Tyr Arg Gln Gln Arg Met Ser Lys Thr Ala Asn Asp Asn Asn  
485 490 495

Asn Ser Glu Phe Ala Trp Thr Ala Ala Thr Lys Tyr Tyr Leu Asn Gly  
500 505 510

25 Arg Asn Ser Leu Val Asn Pro Gly Pro Pro Val Ala Ser His Lys Asp  
515 520 525

30 Asp Glu Glu Lys Tyr Phe Pro Met His Gly Asn Leu Ile Phe Gly Lys  
530 535 540

Gln Gly Thr Gly Thr Thr Asn Val Asp Ile Glu Ser Val Leu Ile Thr  
545 550 555 560

35 Asp Glu Glu Glu Ile Arg Thr Thr Asn Pro Val Ala Thr Glu Gln Tyr  
565 570 575

40 Gly Gln Val Ala Thr Asn His Gln Ser Gln Asn Thr Thr Ala Ser Tyr  
580 585 590

Gly Ser Val Asp Ser Gln Gly Ile Leu Pro Gly Met Val Trp Gln Asp  
595 600 605

45 Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Thr Pro His Thr  
610 615 620

50 Asp Gly His Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu Lys  
625 630 635 640

His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala Asn  
645 650 655

55



# EP 1 310 571 B1

5 Pro Ala Thr Thr Phe Thr Pro Gly Lys Phe Ala Ser Phe Ile Thr Gln  
660 665 670

Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln Lys  
675 680 685

10 Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn Tyr  
690 695 700

15 Asn Lys Ser Val Asn Val Glu Phe Thr Val Asp Ala Asn Gly Val Tyr  
705 710 715 720

Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu  
725 730 735

20  
<210> 67  
<211> 735  
<212> PRT  
<213> capsid protein of AAV serotype, clone A3.7  
25  
<400> 67

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55

EP 1 310 571 B1

	Met	Ala	Ala	Asp	Gly	Tyr	Leu	Pro	Asp	Trp	Leu	Glu	Asp	Thr	Leu	Ser
	1				5					10					15	
5	Glu	Gly	Ile	Arg	Gln	Trp	Trp	Lys	Leu	Lys	Pro	Gly	Pro	Pro	Pro	Pro
				20					25					30		
	Lys	Pro	Asn	Gln	Gln	His	Arg	Asp	Asp	Ser	Arg	Gly	Leu	Val	Leu	Pro
10			35					40					45			
	Gly	Tyr	Lys	Tyr	Leu	Gly	Pro	Phe	Asn	Gly	Leu	Asp	Lys	Gly	Glu	Pro
		50					55					60				
15	Val	Asn	Glu	Ala	Asp	Ala	Ala	Ala	Leu	Glu	His	Asp	Lys	Ala	Tyr	Asp
	65					70					75					80
	His	Gln	Leu	Lys	Gln	Gly	Asp	Asn	Pro	Tyr	Leu	Lys	Tyr	Asn	His	Ala
20					85					90					95	
	Asp	Ala	Glu	Phe	Gln	Glu	Arg	Leu	Gln	Glu	Asp	Thr	Ser	Phe	Gly	Gly
				100					105					110		
25	Asn	Leu	Gly	Arg	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Val	Leu	Glu	Pro
			115					120					125			
	Leu	Gly	Leu	Val	Glu	Glu	Ala	Val	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Arg
30		130					135					140				
	Pro	Ile	Glu	Gln	Ser	Pro	Ala	Glu	Pro	Asp	Ser	Ser	Ser	Gly	Ile	Gly
	145					150					155					160

EP 1 310 571 B1

5 Lys Ser Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln Thr  
 165 170 175  
 Gly Asp Thr Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro Pro  
 180 185 190  
 10 Ala Ala Pro Ser Gly Val Gly Ser Asn Thr Met Ala Ser Gly Gly Gly  
 195 200 205  
 Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ser  
 210 215 220  
 15 Ser Gly Asn Trp His Cys Asp Ser Thr Trp Met Gly Asp Arg Val Ile  
 225 230 235 240  
 20 Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn Arg Leu  
 245 250 255  
 Tyr Lys Gln Ile Ser Ser Glu Ser Gly Ala Thr Asn Asp Asn His Tyr  
 260 265 270  
 25 Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His  
 275 280 285  
 30 Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp  
 290 295 300  
 Gly Phe Arg Pro Lys Lys Leu Asn Phe Lys Leu Phe Asn Ile Gln Val  
 305 310 315 320  
 35 Lys Glu Val Thr Gln Asn Asp Gly Thr Thr Thr Ile Ala Asn Asn Leu  
 325 330 335  
 40 Thr Ser Thr Val Gln Val Phe Thr Asp Ser Glu Tyr Gln Leu Pro Tyr  
 340 345 350  
 Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp  
 355 360 365  
 45 Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser  
 370 375 380  
 50 Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser  
 385 390 395 400  
 Gln Met Leu Arg Thr Gly Asn Asn Phe Thr Phe Ser Tyr Thr Phe Glu  
 405 410 415  
 55

EP 1 310 571 B1

Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg  
 420 425 430  
 5  
 Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ser Lys Thr  
 435 440 445  
 Gln Gly Thr Ser Gly Thr Thr Gln Gln Ser Arg Leu Gln Phe Ser Gln  
 450 455 460  
 10  
 Ala Gly Pro Ser Ser Met Ala Gln Gln Ala Lys Asn Trp Leu Pro Gly  
 465 470 475 480  
 15  
 Pro Ser Tyr Arg Gln Gln Arg Met Ser Lys Thr Ala Asn Asp Asn Asn  
 485 490 495  
 Asn Ser Glu Phe Ala Trp Thr Ala Ala Thr Lys Tyr Tyr Leu Asn Gly  
 500 505 510  
 20  
 Arg Asn Ser Leu Val Asn Pro Gly Pro Pro Met Ala Ser His Lys Asp  
 515 520 525  
 25  
 Asp Glu Glu Lys Tyr Phe Pro Met His Gly Asn Leu Ile Phe Gly Lys  
 530 535 540  
 Gln Gly Thr Gly Thr Thr Asn Val Asp Ile Glu Ser Val Leu Ile Thr  
 545 550 555 560  
 30  
 Asp Glu Glu Glu Ile Arg Thr Thr Asn Pro Val Ala Thr Glu Gln Tyr  
 565 570 575  
 35  
 Gly Gln Val Ala Thr Asn His Gln Ser Gln Asn Thr Thr Ala Ser Tyr  
 580 585 590  
 Gly Ser Val Asp Ser Gln Gly Ile Leu Pro Gly Met Val Trp Gln Asp  
 595 600 605  
 40  
 Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Thr Pro His Thr  
 610 615 620  
 45  
 Asp Gly His Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu Lys  
 625 630 635 640  
 His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala Asn  
 645 650 655  
 50  
 Pro Ala Thr Thr Phe Thr Pro Gly Lys Phe Ala Ser Phe Ile Thr Gln  
 660 665 670  
 55

EP 1 310 571 B1

Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln Lys  
 675 680 685  
 5  
 Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn Tyr  
 690 695 700  
 10  
 Asn Lys Ser Val Asn Val Glu Phe Thr Val Asp Ala Asn Gly Val Tyr  
 705 710 715 720  
 Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu  
 725 730 735  
 15  
 <210> 68  
 <211> 735  
 <212> PRT  
 <213> capsid protein of AAV serotype, clone A3.4  
 20  
 <400> 68  
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 Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Thr Leu Ser  
 1 5 10 15  
 Glu Gly Ile Arg Gln Trp Trp Lys Leu Lys Pro Gly Pro Pro Pro Pro  
 20 25 30  
 30  
 Lys Pro Asn Gln Gln His Arg Asp Asp Ser Arg Gly Leu Val Leu Pro  
 35 40 45  
 Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
 50 55 60  
 35  
 Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
 65 70 75 80  
 40  
 His Gln Leu Lys Gln Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala  
 85 90 95  
 Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
 100 105 110  
 45  
 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
 115 120 125  
 50  
 Leu Gly Leu Val Glu Glu Ala Val Lys Thr Ala Pro Gly Lys Lys Arg  
 130 135 140  
 Pro Ile Glu Gln Ser Pro Ala Glu Pro Asp Ser Ser Ser Gly Ile Gly  
 145 150 155 160  
 55  
 Glu Ser Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln Thr  
 165 170 175

EP 1 310 571 B1

5 Gly Asp Thr Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro Pro  
180 185 190

Ala Ala Pro Ser Gly Val Gly Ser Asn Thr Met Ala Ser Gly Gly Gly  
195 200 205

10 Ala Pro Met Ala Asp Asp Asn Glu Gly Ala Asp Gly Val Gly Asn Ser  
210 215 220

Ser Gly Asn Trp His Cys Asp Ser Thr Trp Met Gly Asp Arg Val Ile  
225 230 235 240

15 Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu  
245 250 255

20 Tyr Lys Gln Ile Ser Ser Glu Ser Gly Ala Thr Asn Asp Asn His Tyr  
260 265 270

Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His  
275 280 285

25 Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp  
290 295 300

30 Gly Phe Arg Pro Lys Lys Leu Asn Phe Lys Leu Phe Asn Ile Gln Val  
305 310 315 320

Lys Glu Val Thr Gln Asn Asp Gly Thr Thr Thr Ile Ala Asn Asn Leu  
325 330 335

35 Thr Ser Thr Val Gln Val Phe Thr Asp Ser Glu Tyr Gln Leu Pro Tyr  
340 345 350

40 Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp  
355 360 365

Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser  
370 375 380

45 Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser  
385 390 395 400

50 Gln Met Leu Arg Thr Gly Asn Asn Phe Thr Phe Ser Tyr Thr Phe Glu  
405 410 415

Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg  
420 425 430

55

EP 1 310 571 B1

5 Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ser Lys Thr  
435 440 445

Gln Gly Thr Ser Gly Thr Thr Gln Gln Ser Arg Leu Gln Phe Ser Gln  
450 455 460

10 Ala Gly Pro Ser Ser Met Ala Gln Gln Ala Lys Asn Trp Leu Pro Gly  
465 470 475 480

15 Pro Ser Tyr Arg Gln Gln Arg Met Ser Lys Thr Ala Asn Asp Asn Asn  
485 490 495

Asn Ser Glu Phe Ala Trp Thr Ala Ala Thr Lys Tyr Tyr Leu Asn Gly  
500 505 510

20 Arg Asn Ser Leu Val Asn Pro Gly Pro Pro Met Ala Ser His Lys Asp  
515 520 525

25 Asp Glu Glu Lys Tyr Phe Pro Met His Gly Asn Leu Ile Phe Gly Lys  
530 535 540

Gln Gly Thr Gly Thr Thr Asn Val Asp Ile Glu Ser Val Leu Ile Thr  
545 550 555 560

30 Asp Glu Glu Glu Ile Arg Thr Thr Asn Pro Val Ala Thr Glu Gln Tyr  
565 570 575

Gly Gln Val Ala Thr Asn His Gln Ser Gln Asp Thr Thr Ala Ser Tyr  
580 585 590

35 Gly Ser Val Asp Ser Gln Gly Ile Leu Pro Gly Met Val Trp Gln Asp  
595 600 605

40 Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Thr Pro His Thr  
610 615 620

45 Asp Gly His Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu Lys  
625 630 635 640

His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala Asn  
645 650 655

50 Pro Ala Thr Thr Phe Thr Pro Gly Lys Phe Ala Ser Phe Ile Thr Gln  
660 665 670

55 Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln Lys  
675 680 685

# EP 1 310 571 B1

Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn Tyr  
690 695 700

5

Asn Lys Ser Val Asn Val Glu Phe Thr Val Asp Ala Asn Gly Val Tyr  
705 710 715 720

10

Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu  
725 730 735

<210> 69

<211> 735

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<212> PRT

<213> capsid protein of AAV serotype, clone A3.5

<400> 69

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EP 1 310 571 B1

	Met	Ala	Ala	Asp	Gly	Tyr	Leu	Pro	Asp	Trp	Leu	Glu	Asp	Thr	Leu	Ser
	1				5					10					15	
5	Glu	Gly	Ile	Arg	Gln	Trp	Trp	Lys	Leu	Lys	Pro	Gly	Pro	Pro	Pro	Pro
				20					25				30			
	Lys	Pro	Asn	Gln	Gln	His	Arg	Asp	Asp	Ser	Arg	Gly	Leu	Val	Leu	Pro
10			35					40					45			
	Gly	Tyr	Lys	Tyr	Leu	Gly	Pro	Phe	Asn	Gly	Leu	Asp	Lys	Gly	Glu	Pro
		50					55					60				
15	Val	Asn	Glu	Ala	Asp	Ala	Ala	Ala	Leu	Glu	His	Asp	Lys	Ala	Tyr	Asp
	65					70					75					80
	His	Gln	Leu	Lys	Gln	Gly	Asp	Asn	Pro	Tyr	Leu	Lys	Tyr	Asn	His	Ala
20					85					90					95	
	Asp	Ala	Glu	Phe	Gln	Glu	Arg	Leu	Gln	Glu	Asp	Thr	Ser	Phe	Gly	Gly
				100					105					110		
25	Asn	Leu	Gly	Arg	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Val	Leu	Glu	Pro
			115					120					125			
	Leu	Gly	Leu	Val	Glu	Glu	Ala	Val	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Arg
30		130					135					140				
	Pro	Ile	Glu	Gln	Ser	Pro	Ala	Glu	Pro	Asp	Ser	Ser	Ser	Gly	Ile	Gly
	145					150					155					160
35	Lys	Ser	Gly	Gln	Gln	Pro	Ala	Lys	Lys	Arg	Leu	Asn	Phe	Gly	Gln	Thr
				165						170					175	
	Gly	Asp	Thr	Glu	Ser	Val	Pro	Asp	Pro	Gln	Pro	Ile	Gly	Glu	Pro	Pro
40				180					185					190		
45																
50																
55																

EP 1 310 571 B1

Ala Ala Pro Ser Gly Val Gly Ser Asn Thr Met Ala Ser Gly Gly Gly  
195 200 205

5 Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ser  
210 215 220

10 Ser Gly Asn Trp His Cys Asp Ser Thr Trp Met Gly Asp Arg Val Ile  
225 230 235 240

Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu  
245 250 255

15 Tyr Lys Gln Ile Ser Ser Glu Ser Gly Ala Thr Asn Asp Asn His Tyr  
260 265 270

20 Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His  
275 280 285

Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp  
290 295 300

25 Gly Phe Arg Pro Lys Lys Leu Asn Phe Lys Leu Phe Asn Ile Gln Val  
305 310 315 320

30 Lys Glu Val Thr Gln Asn Asp Gly Thr Thr Thr Ile Ala Asn Asn Leu  
325 330 335

Thr Ser Thr Val Gln Val Phe Thr Asp Ser Glu Tyr Gln Leu Pro Tyr  
340 345 350

35 Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp  
355 360 365

40 Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser  
370 375 380

Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser  
385 390 395 400

45 Gln Met Leu Arg Thr Gly Asn Asn Phe Thr Phe Ser Tyr Thr Phe Glu  
405 410 415

50 Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg  
420 425 430

Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ser Lys Thr  
435 440 445

55

EP 1 310 571 B1

Gln Gly Thr Ser Gly Thr Thr Gln Gln Ser Arg Leu Gln Phe Asn Gln.  
 450 455 460  
 5  
 Ala Gly Pro Ser Ser Met Ala Gln Gln Ala Lys Asn Trp Leu Pro Gly  
 465 470 475 480  
 10  
 Pro Ser Tyr Arg Gln Gln Arg Met Ser Lys Thr Ala Asn Asp Asn Asn  
 485 490 495  
 Asn Ser Glu Phe Ala Trp Thr Ala Ala Thr Lys Tyr Tyr Pro Asn Gly  
 500 505 510  
 15  
 Arg Asn Ser Leu Val Asn Pro Gly Pro Pro Met Ala Ser His Lys Asp  
 515 520 525  
 20  
 Asp Glu Glu Lys Tyr Phe Pro Met His Gly Asn Leu Ile Phe Gly Lys  
 530 535 540  
 Gln Gly Thr Gly Thr Thr Asn Val Asp Ile Glu Ser Val Leu Ile Thr  
 545 550 555 560  
 25  
 Asp Glu Glu Glu Ile Arg Thr Thr Asn Pro Val Ala Thr Glu Gln Tyr  
 565 570 575  
 Gly Gln Val Ala Thr Asn Arg Gln Ser Gln Asn Thr Thr Ala Ser Tyr  
 580 585 590  
 30  
 Gly Ser Val Asp Ser Gln Gly Ile Leu Pro Gly Met Val Trp Gln Asp  
 595 600 605  
 35  
 Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Thr Pro His Thr  
 610 615 620  
 Asp Gly His Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu Lys  
 625 630 635 640  
 40  
 His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala Asn  
 645 650 655  
 45  
 Pro Ala Thr Thr Phe Thr Pro Gly Lys Phe Ala Ser Phe Ile Thr Gln  
 660 665 670  
 Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln Lys  
 675 680 685  
 50  
 Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn Tyr  
 690 695 700  
 55

# EP 1 310 571 B1

Asn Lys Ser Val Asn Val Glu Phe Thr Val Asp Ala Asn Gly Val Tyr  
705 710 715 720

Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu  
725 730 735

<210> 70  
<211> 735  
<212> PRT  
<213> capsid protein of AAV serotype, clone AAV2

<400> 70

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Thr Leu Ser  
1 5 10 15

Glu Gly Ile Arg Gln Trp Trp Lys Leu Lys Pro Gly Pro Pro Pro Pro  
20 25 30

Lys Pro Ala Glu Arg His Lys Asp Asp Ser Arg Gly Leu Val Leu Pro  
25 35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60

Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

Arg Gln Leu Asp Ser Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala  
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Lys Glu Asp Thr Ser Phe Gly Gly  
100 105 110

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
115 120 125

Leu Gly Leu Val Glu Glu Pro Val Lys Thr Ala Pro Gly Lys Lys Arg  
130 135 140

Pro Val Glu His Ser Pro Val Glu Pro Asp Ser Ser Ser Gly Thr Gly  
145 150 155 160

Lys Ala Gly Gln Gln Pro Ala Arg Lys Arg Leu Asn Phe Gly Gln Thr  
165 170 175

Gly Asp Ala Asp Ser Val Pro Asp Pro Gln Pro Leu Gly Gln Pro Pro  
180 185 190

EP 1 310 571 B1

Ala Ala Pro Ser Gly Leu Gly Thr Asn Thr Met Ala Thr Gly Ser Gly  
195 200 205

5  
Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ser  
210 215 220

10  
Ser Gly Asn Trp His Cys Asp Ser Thr Trp Met Gly Asp Arg Val Ile  
225 230 235 240

15  
Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu  
245 250 255

20  
Tyr Lys Gln Ile Ser Ser Gln Ser Gly Ala Ser Asn Asp Asn His Tyr  
260 265 270

25  
Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His  
275 280 285

30  
Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp  
290 295 300

35  
Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn Ile Gln Val  
305 310 315 320

40  
Lys Glu Val Thr Gln Asn Asp Gly Thr Thr Thr Ile Ala Asn Asn Leu  
325 330 335

45  
Thr Ser Thr Val Gln Val Phe Thr Asp Ser Glu Tyr Gln Leu Pro Tyr  
340 345 350

50  
Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp  
355 360 365

55  
Val Phe Met Val Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser  
370 375 380

Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser  
385 390 395 400

Gln Met Leu Arg Thr Gly Asn Asn Phe Thr Phe Ser Tyr Thr Phe Glu  
405 410 415

Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg  
420 425 430

Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ser Arg Thr  
435 440 445

EP 1 310 571 B1

5 Asn Thr Pro Ser Gly Thr Thr Thr Gln Ser Arg Leu Gln Phe Ser Gln  
 450 455 460  
 Ala Gly Ala Ser Asp Ile Arg Asp Gln Ser Arg Asn Trp Leu Pro Gly  
 465 470 475 480  
 10 Pro Cys Tyr Arg Gln Gln Arg Val Ser Lys Thr Ser Ala Asp Asn Asn  
 485 490 495  
 Asn Ser Glu Tyr Ser Trp Thr Gly Ala Thr Lys Tyr His Leu Asn Gly  
 500 505 510  
 15 Arg Asp Ser Leu Val Asn Pro Gly Pro Ala Met Ala Ser His Lys Asp  
 515 520 525  
 Asp Glu Glu Lys Phe Phe Pro Gln Ser Gly Val Leu Ile Phe Gly Lys  
 530 535 540  
 20 Gln Gly Ser Glu Lys Thr Asn Val Asp Ile Glu Lys Val Met Ile Thr  
 545 550 555 560  
 25 Asp Glu Glu Glu Ile Arg Thr Thr Asn Pro Val Ala Thr Glu Gln Tyr  
 565 570 575  
 Gly Ser Val Ser Thr Asn Leu Gln Arg Gly Asn Arg Gln Ala Ala Thr  
 580 585 590  
 30 Ala Asp Val Asn Thr Gln Gly Val Leu Pro Gly Met Val Trp Gln Asp  
 595 600 605  
 35 Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His Thr  
 610 615 620  
 Asp Gly His Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu Lys  
 625 630 635 640  
 40 His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala Asn  
 645 650 655  
 45 Pro Ser Thr Thr Phe Ser Ala Ala Lys Phe Ala Ser Phe Ile Thr Gln  
 660 665 670  
 Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln Lys  
 675 680 685  
 50 Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn Tyr  
 690 695 700  
 55

# EP 1 310 571 B1

Asn Lys Ser Val Asn Val Asp Phe Thr Val Asp Thr Asn Gly Val Tyr  
705 710 715 720

5

Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu  
725 730 735

<210> 71

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<211> 736

<212> PRT

<213> capsid protein of AAV serotype, clone AAV3

<400> 71

15

20

25

30

35

40

45

50

55

EP 1 310 571 B1

	Met	Ala	Ala	Asp	Gly	Tyr	Leu	Pro	Asp	Trp	Leu	Glu	Asp	Asn	Leu	Ser	
	1				5					10					15		
5	Glu	Gly	Ile	Arg	Glu	Trp	Trp	Ala	Leu	Lys	Pro	Gly	Val	Pro	Gln	Pro	
				20					25					30			
	Lys	Ala	Asn	Gln	Gln	His	Gln	Asp	Asn	Arg	Arg	Gly	Leu	Val	Leu	Pro	
10			35					40					45				
	Gly	Tyr	Lys	Tyr	Leu	Gly	Pro	Gly	Asn	Gly	Leu	Asp	Lys	Gly	Glu	Pro	
		50					55					60					
15	Val	Asn	Glu	Ala	Asp	Ala	Ala	Ala	Leu	Glu	His	Asp	Lys	Ala	Tyr	Asp	
	65					70					75					80	
	Gln	Gln	Leu	Lys	Ala	Gly	Asp	Asn	Pro	Tyr	Leu	Lys	Tyr	Asn	His	Ala	
20					85					90					95		
	Asp	Ala	Glu	Phe	Gln	Glu	Arg	Leu	Gln	Glu	Asp	Thr	Ser	Phe	Gly	Gly	
				100					105					110			
25	Asn	Leu	Gly	Arg	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Ile	Leu	Glu	Pro	
			115					120					125				
	Leu	Gly	Leu	Val	Glu	Glu	Ala	Ala	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Gly	
30		130					135					140					
	Ala	Val	Asp	Gln	Ser	Pro	Gln	Glu	Pro	Asp	Ser	Ser	Ser	Gly	Val	Gly	
	145					150					155					160	
35	Lys	Ser	Gly	Lys	Gln	Pro	Ala	Arg	Lys	Arg	Leu	Asn	Phe	Gly	Gln	Thr	
					165					170					175		
	Gly	Asp	Ser	Glu	Ser	Val	Pro	Asp	Pro	Gln	Pro	Leu	Gly	Glu	Pro	Pro	
40				180					185					190			
	Ala	Ala	Pro	Thr	Ser	Leu	Gly	Ser	Asn	Thr	Met	Ala	Ser	Gly	Gly	Gly	
			195					200					205				



EP 1 310 571 B1

5  
Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ser  
210 215 220

10  
Ser Gly Asn Trp His Cys Asp Ser Gln Trp Leu Gly Asp Arg Val Ile  
225 230 235 240

15  
Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu  
245 250 255

20  
Tyr Lys Gln Ile Ser Ser Gln Ser Gly Ala Ser Asn Asp Asn His Tyr  
260 265 270

25  
Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His  
275 280 285

30  
Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp  
290 295 300

35  
Gly Phe Arg Pro Lys Lys Leu Ser Phe Lys Leu Phe Asn Ile Gln Val  
305 310 315 320

40  
Arg Gly Val Thr Gln Asn Asp Gly Thr Thr Thr Ile Ala Asn Asn Leu  
325 330 335

45  
Thr Ser Thr Val Gln Val Phe Thr Asp Ser Glu Tyr Gln Leu Pro Tyr  
340 345 350

50  
Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp  
355 360 365

55  
Val Phe Met Val Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser  
370 375 380

60  
Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser  
385 390 395 400

65  
Gln Met Leu Arg Thr Gly Asn Asn Phe Gln Phe Ser Tyr Thr Phe Glu  
405 410 415

70  
Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg  
420 425 430

75  
Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Asn Arg Thr  
435 440 445

80  
Gln Gly Thr Thr Ser Gly Thr Thr Asn Gln Ser Arg Leu Leu Phe Ser  
450 455 460

EP 1 310 571 B1

5 Gln Ala Gly Pro Gln Ser Met Ser Leu Gln Ala Arg Asn Trp Leu Pro  
465 470 475 480

Gly Pro Cys Tyr Arg Gln Gln Arg Leu Ser Lys Thr Ala Asn Asp Asn  
485 490 495

10 Asn Asn Ser Asn Phe Pro Trp Thr Ala Ala Ser Lys Tyr His Leu Asn  
500 505 510

Gly Arg Asp Ser Leu Val Asn Pro Gly Pro Ala Met Ala Ser His Lys  
515 520 525

Asp Asp Glu Glu Lys Phe Phe Pro Met His Gly Asn Leu Ile Phe Gly  
530 535 540

20 Lys Glu Gly Thr Thr Ala Ser Asn Ala Glu Leu Asp Asn Val Met Ile  
545 550 555 560

Thr Asp Glu Glu Glu Ile Arg Thr Thr Asn Pro Val Ala Thr Glu Gln  
565 570 575

25 Tyr Gly Thr Val Ala Asn Asn Leu Gln Ser Ser Asn Thr Ala Pro Thr  
580 585 590

30 Thr Gly Thr Val Asn His Gln Gly Ala Leu Pro Gly Met Val Trp Gln  
595 600 605

Asp Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His  
610 615 620

35 Thr Asp Gly His Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu  
625 630 635 640

40 Lys His Pro Pro Pro Gln Ile Met Ile Lys Asn Thr Pro Val Pro Ala  
645 650 655

Asn Pro Pro Thr Thr Phe Ser Pro Ala Lys Phe Ala Ser Phe Ile Thr  
660 665 670

45 Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln  
675 680 685

50 Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn  
690 695 700

55 Tyr Asn Lys Ser Val Asn Val Asp Phe Thr Val Asp Thr Asn Gly Val  
705 710 715 720

# EP 1 310 571 B1

Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu  
725 730 735

5

<210> 72

<211> 737

<212> PRT

<213> capsid protein of AAV serotype, clone 3.3bVP1

10

<400> 72

15

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
1 5 10 15

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
20 25 30

20

Lys Ala Asn Gln Gln Lys Gln Asp Asn Gly Arg Gly Leu Val Leu Pro  
35 40 45

25

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60

Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

30

Gln Gln Leu Asn Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
85 90 95

35

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
100 105 110

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
115 120 125

40

Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Ala Lys Lys Arg  
130 135 140

45

Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile  
145 150 155 160

Gly Lys Lys Gly Gln Gln Pro Ala Arg Lys Arg Leu Asn Phe Gly Gln  
165 170 175

50

Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro  
180 185 190

55

Pro Ala Ala Pro Ser Ser Val Gly Ser Gly Thr Val Ala Ala Gly Gly  
195 200 205

EP 1 310 571 B1

Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn  
 210 215 220  
 5  
 Ala Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val  
 225 230 235 240  
 10  
 Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His  
 245 250 255  
 Leu Tyr Glu Gln Ile Ser Ser Glu Thr Ala Gly Ser Thr Asn Asp Asn  
 260 265 270  
 15  
 Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg  
 275 280 285  
 Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn  
 290 295 300  
 20  
 Asn Trp Gly Phe Arg Pro Lys Lys Leu Arg Phe Lys Leu Phe Asn Ile  
 305 310 315 320  
 25  
 Gln Val Lys Glu Val Thr Thr Asn Asp Gly Val Thr Thr Ile Ala Asn  
 325 330 335  
 Asn Leu Thr Ser Thr Ile Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu  
 340 345 350  
 30  
 Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro  
 355 360 365  
 35  
 Ala Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn  
 370 375 380  
 Gly Ser Gln Ser Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe  
 385 390 395 400  
 40  
 Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr Ser  
 405 410 415  
 45  
 Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu  
 420 425 430  
 Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala  
 435 440 445  
 50  
 Arg Thr Gln Ser Asp Pro Gly Gly Thr Ala Gly Asn Arg Glu Leu Gln  
 450 455 460  
 55

EP 1 310 571 B1

5 Phe Tyr Gln Gly Gly Pro Ser Thr Met Ala Glu Gln Ala Lys Asn Trp  
465 470 475 480

10 Leu Pro Gly Pro Cys Phe Arg Gln Gln Arg Val Ser Lys Thr Leu Asp  
485 490 495

15 Gln Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His  
500 505 510

20 Leu Asn Gly Arg Asn Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr  
515 520 525

25 His Lys Asp Asp Glu Asp Arg Phe Phe Pro Ser Ser Gly Val Leu Ile  
530 535 540

30 Phe Gly Lys Thr Gly Ala Thr Asn Lys Thr Thr Leu Glu Asn Val Leu  
545 550 555 560

35 Met Thr Asn Glu Glu Glu Ile Arg Pro Thr Asn Pro Val Ala Thr Glu  
565 570 575

40 Glu Tyr Gly Ile Val Ser Ser Asn Leu Gln Ala Ala Asn Thr Ala Ala  
580 585 590

45 Gln Thr Gln Val Val Asn Asn Gln Gly Ala Leu Pro Gly Met Val Trp  
595 600 605

50 Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro  
610 615 620

55 His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly  
625 630 635 640

60 Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro  
645 650 655

65 Ala Asn Pro Pro Glu Val Phe Thr Pro Ala Lys Phe Ala Ser Phe Ile  
660 665 670

70 Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu  
675 680 685

75 Gln Lys Glu Asn Ser Lys Arg Trp Asp Pro Glu Ile Gln Tyr Thr Ser  
690 695 700

80 Asn Phe Glu Lys Gln Thr Gly Val Asp Phe Ala Val Asp Ser Gln Gly  
705 710 715 720

# EP 1 310 571 B1

Val Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn  
725 730 735

5

Leu

<210> 73

10 <211> 644

<212> PRT

<213> capsid protein of AAV serotype, clone 223-4

<400> 73

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Lys Ala Tyr Asp Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg  
1 5 10 15

20

Tyr Asn His Ala Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr  
20 25 30

Ser Phe Gly Gly Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg  
35 40 45

25

Val Leu Glu Pro Leu Gly Leu Val Glu Thr Pro Ala Lys Thr Ala Pro  
50 55 60

30

Gly Lys Lys Arg Pro Val Asp Ser Pro Asp Ser Thr Ser Gly Ile Gly  
65 70 75 80

Lys Lys Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln Thr  
85 90 95

35

Gly Asp Ser Glu Pro Val Pro Asp Pro Gln Pro Ile Gly Glu Pro Pro  
100 105 110

40

Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly Gly  
115 120 125

Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala  
130 135 140

45

Ser Gly Asn Trp His Cys Asp Ser Thr Arg Leu Gly Asp Arg Val Ile  
145 150 155 160

50

Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu  
165 170 175

Tyr Lys Gln Ile Ser Ser Gln Ser Ala Gly Ser Thr Asn Asp Asn Val  
180 185 190

55

Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe  
195 200 205

EP 1 310 571 B1

5  
His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn  
210 215 220

10  
Trp Gly Phe Arg Pro Lys Lys Leu Asn Phe Lys Leu Phe Asn Ile Gln  
225 230 235 240

15  
Val Lys Glu Val Thr Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn  
245 250 255

20  
Leu Thr Ser Thr Val Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro  
260 265 270

25  
Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala  
275 280 285

30  
Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly  
290 295 300

35  
Ser Gln Ser Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro  
305 310 315 320

40  
Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Thr Phe Ser Tyr Thr Phe  
325 330 335

45  
Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Gly  
340 345 350

50  
Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala Arg  
355 360 365

55  
Thr Gln Ser Asn Ala Gly Gly Thr Ala Gly Asn Arg Glu Leu Gln Phe  
370 375 380

60  
Tyr Gln Gly Gly Pro Thr Thr Met Ala Glu Gln Ala Lys Asn Trp Leu  
385 390 395 400

65  
Pro Gly Pro Cys Phe Arg Gln Gln Arg Val Ser Lys Thr Leu Asp Gln  
405 410 415

70  
Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His Leu  
420 425 430

75  
Asn Gly Arg Asn Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr His  
435 440 445

80  
Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Ile Phe  
450 455 460

# EP 1 310 571 B1

5 Gly Lys Thr Gly Ala Ala Asn Lys Thr Thr Leu Glu Asn Val Leu Met  
465 470 475 480

Thr Asn Glu Glu Glu Ile Arg Pro Thr Asn Pro Val Ala Thr Glu Glu  
485 490 495

10 Tyr Gly Ile Val Ser Ser Asn Leu Gln Ala Ala Ser Thr Ala Ala Gln  
500 505 510

Thr Gln Val Val Asn Asn Gln Gly Ala Leu Pro Gly Met Val Trp Gln  
515 520 525

15 Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His  
530 535 540

20 Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu  
545 550 555 560

Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala  
565 570 575

25 Asn Pro Pro Glu Val Phe Thr Pro Ala Lys Phe Ala Ser Phe Ile Thr  
580 585 590

30 Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln  
595 600 605

Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn  
610 615 620

35 Phe Asp Lys Gln Thr Gly Val Asp Phe Ala Val Asp Ser Gln Gly Val  
625 630 635 640

40 Tyr Ser Glu Pro

<210> 74

<211> 644

<212> PRT

<213> capsid protein of AAV serotype, clone 223.5

<400> 74



# EP 1 310 571 B1

Lys Ala Tyr Asp Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg  
 1 5 10 15

5 Tyr Asn His Ala Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr  
 20 25 30

10 Ser Phe Gly Gly Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg  
 35 40 45

15

20

25

30

35

40

45

50

55

EP 1 310 571 B1

Val Leu Glu Pro Leu Gly Leu Val Glu Thr Pro Ala Lys Thr Ala Pro  
50 55 60

5 Gly Lys Lys Arg Pro Val Asp Ser Pro Asp Ser Thr Ser Gly Ile Gly  
65 70 75 80

10 Lys Lys Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln Thr  
85 90 95

Gly Asp Ser Glu Pro Val Pro Asp Pro Gln Pro Ile Gly Glu Pro Pro  
100 105 110

15 Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly Gly  
115 120 125

20 Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala  
130 135 140

Ser Gly Asn Trp His Cys Asp Ser Thr Arg Leu Gly Asp Arg Val Ile  
145 150 155 160

25 Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu  
165 170 175

30 Tyr Lys Gln Ile Ser Ser Gln Ser Ala Gly Ser Thr Asn Asp Asn Val  
180 185 190

Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe  
195 200 205

35 His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn  
210 215 220

40 Trp Gly Phe Arg Pro Lys Lys Leu Asn Phe Lys Leu Phe Asn Ile Gln  
225 230 235 240

Val Lys Glu Val Thr Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn  
245 250 255

45 Leu Thr Ser Thr Val Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro  
260 265 270

50 Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala  
275 280 285

Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly  
290 295 300

EP 1 310 571 B1

	Ser	Gln	Ser	Val	Gly	Arg	Ser	Ser	Phe	Tyr	Cys	Leu	Glu	Tyr	Phe	Pro
	305					310					315					320
5	Ser	Gln	Met	Leu	Arg	Thr	Gly	Asn	Asn	Phe	Thr	Phe	Ser	Tyr	Thr	Phe
					325					330					335	
10	Glu	Asp	Val	Pro	Phe	His	Ser	Ser	Tyr	Ala	His	Ser	Gln	Ser	Leu	Gly
				340					345					350		
15	Arg	Leu	Met	Asn	Pro	Leu	Ile	Asp	Gln	Tyr	Leu	Tyr	Tyr	Leu	Ala	Arg
			355					360					365			
20	Thr	Gln	Ser	Asn	Ala	Gly	Gly	Thr	Ala	Gly	Asn	Arg	Glu	Leu	Gln	Phe
	370						375					380				
25	Tyr	Gln	Gly	Gly	Pro	Thr	Thr	Met	Ala	Glu	Gln	Ala	Lys	Asn	Trp	Leu
	385					390					395					400
30	Pro	Gly	Pro	Cys	Phe	Arg	Gln	Gln	Arg	Val	Ser	Lys	Thr	Leu	Asp	Gln
					405					410					415	
35	Asn	Asn	Asn	Ser	Asn	Phe	Ala	Trp	Thr	Gly	Ala	Thr	Lys	Tyr	His	Leu
				420					425					430		
40	Asn	Gly	Arg	Asn	Ser	Leu	Val	Asn	Pro	Gly	Val	Ala	Met	Ala	Thr	His
			435					440					445			
45	Lys	Asp	Asp	Glu	Glu	Arg	Phe	Phe	Pro	Ser	Ser	Gly	Val	Leu	Ile	Phe
	450						455					460				
50	Gly	Lys	Thr	Gly	Ala	Ala	Asn	Lys	Thr	Thr	Leu	Glu	Asn	Val	Leu	Met
	465					470					475					480
55	Thr	Asn	Glu	Glu	Glu	Ile	Arg	Pro	Thr	Asn	Pro	Val	Ala	Thr	Glu	Glu
					485				490						495	
60	Tyr	Gly	Ile	Val	Ser	Ser	Asn	Leu	Gln	Ala	Ala	Ser	Thr	Ala	Ala	Gln
				500				505						510		
65	Thr	Gln	Val	Val	Asn	Asn	Gln	Gly	Ala	Leu	Pro	Gly	Met	Val	Trp	Gln
			515					520					525			
70	Asn	Arg	Asp	Val	Tyr	Leu	Gln	Gly	Pro	Ile	Trp	Ala	Lys	Ile	Pro	His
	530						535					540				
75	Thr	Asp	Gly	Asn	Phe	His	Pro	Ser	Pro	Leu	Met	Gly	Gly	Phe	Gly	Leu
	545					550					555					560

# EP 1 310 571 B1

Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala  
 565 570 575  
 5 Asn Pro Pro Glu Val Phe Thr Pro Ala Lys Phe Ala Ser Phe Ile Thr  
 580 585 590  
 10 Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln  
 595 600 605  
 Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn  
 610 615 620  
 15 Phe Asp Lys Gln Thr Gly Val Asp Phe Ala Val Asp Ser Gln Gly Val  
 625 630 635 640  
 Tyr Ser Glu Pro  
 20  
 <210> 75  
 <211> 644  
 <212> PRT  
 25 <213> capsid protein of AAV serotype, clone 223.10  
 <220>  
 <221> MISC\_FEATURE  
 <222> (434)..(434)  
 30 <223> can be any amino acid  
 <400> 75  
 35 Lys Ala Tyr Asp Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg  
 1 5 10 15  
 Tyr Asn His Ala Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr  
 20 25 30  
 40 Ser Phe Gly Gly Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg  
 35 40 45  
 45 Val Leu Glu Pro Leu Gly Leu Val Glu Thr Pro Ala Lys Thr Ala Pro  
 50 55 60  
 Gly Lys Lys Arg Pro Val Asp Ser Pro Asp Ser Thr Ser Gly Ile Gly  
 65 70 75 80  
 50 Lys Lys Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln Thr  
 85 90 95  
 55 Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro Pro  
 100 105 110

EP 1 310 571 B1

Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly Gly  
115 120 125

Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala  
130 135 140

Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile  
145 150 155 160

Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu  
165 170 175

Tyr Lys Gln Ile Ser Ser Gln Ser Ala Gly Ser Thr Asn Asp Asn Val  
180 185 190

Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe  
195 200 205

His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn  
210 215 220

Trp Gly Phe Arg Pro Lys Lys Leu Asn Phe Lys Leu Phe Asn Ile Gln  
225 230 235 240

Val Lys Glu Val Thr Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn  
245 250 255

Leu Thr Ser Thr Val Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro  
260 265 270

Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala  
275 280 285

Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly  
290 295 300

Ser Gln Ser Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro  
305 310 315 320

Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Thr Phe Ser Tyr Thr Phe  
325 330 335

Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp  
340 345 350

Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala Arg  
355 360 365

EP 1 310 571 B1

5  
 Thr Gln Ser Asn Ala Gly Gly Thr Ala Gly Asn Arg Glu Leu Gln Phe  
 370 375 380

10  
 Tyr Gln Gly Gly Pro Thr Thr Met Ala Glu Gln Ala Lys Asn Trp Leu  
 385 390 395 400

15  
 Pro Gly Pro Cys Phe Arg Gln Gln Arg Val Ser Lys Thr Leu Asp Gln  
 405 410 415

20  
 Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His Leu  
 420 425 430

25  
 Asn Xaa Arg Asn Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr His  
 435 440 445

30  
 Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Ile Phe  
 450 455 460

35  
 Gly Lys Thr Gly Ala Ala Asn Lys Thr Thr Leu Glu Asn Val Leu Met  
 465 470 475 480

40  
 Thr Asn Glu Glu Glu Ile Arg Pro Thr Asn Pro Val Ala Thr Glu Glu  
 485 490 495

45  
 Tyr Gly Ile Val Ser Ser Asn Leu Gln Ala Ala Ser Thr Ala Ala Gln  
 500 505 510

50  
 Thr Gln Val Val Asn Asn Gln Gly Ala Leu Pro Gly Met Val Trp Gln  
 515 520 525

55  
 Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His  
 530 535 540

60  
 Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu  
 545 550 555 560

65  
 Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala  
 565 570 575

70  
 Asn Pro Pro Glu Val Phe Thr Pro Ala Lys Phe Ala Ser Phe Ile Thr  
 580 585 590

75  
 Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln  
 595 600 605

80  
 Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn  
 610 615 620

EP 1 310 571 B1

5 Phe Asp Lys Gln Thr Gly Val Asp Phe Ala Val Asp Ser Gln Gly Val  
625 630 635 640

Tyr Ser Glu Pro

<210> 76  
 10 <211> 644  
 <212> PRT  
 <213> capsid protein of AAV serotype, clone 223.2

<400> 76

15 Lys Ala Tyr Asp Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg  
1 5 10 15

20 Tyr Asn His Ala Asp Ala Glu Phe Gln Glu Cys Leu Gln Glu Asp Thr  
20 25 30

25 Ser Phe Gly Gly Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg  
35 40 45

30 Val Leu Glu Pro Leu Gly Leu Val Glu Thr Pro Ala Lys Thr Ala Pro  
50 55 60

35 Gly Lys Lys Arg Pro Val Asp Ser Pro Asp Ser Thr Ser Gly Ile Gly  
65 70 75 80

40 Lys Lys Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln Thr  
85 90 95

45 Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro Pro  
100 105 110

50 Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Val Ala Gly Gly Gly  
115 120 125

55 Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala  
130 135 140

Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile  
145 150 155 160

Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu  
165 170 175

Tyr Lys Gln Ile Ser Ser Gln Ser Ala Gly Ser Thr Asn Asp Asn Val  
180 185 190

55 Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe  
195 200 205

EP 1 310 571 B1

5 His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn  
210 215 220

Trp Gly Phe Arg Pro Lys Lys Leu Asn Phe Lys Leu Phe Asn Ile Gln  
225 230 235 240

10 Val Lys Glu Val Thr Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn  
245 250 255

Leu Thr Ser Thr Val Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro  
15 260 265 270

Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala  
275 280 285

20 Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly  
290 295 300

Ser Gln Ser Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro  
25 305 310 315 320

Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Thr Phe Ser Tyr Thr Phe  
325 330 335

30 Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp  
340 345 350

Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala Arg  
35 355 360 365

Thr Gln Ser Asn Ala Gly Gly Thr Ala Gly Asn Arg Glu Leu Gln Phe  
370 375 380

40 Tyr Gln Gly Gly Pro Thr Thr Met Ala Glu Gln Ala Lys Asn Trp Leu  
385 390 395 400

Pro Gly Pro Cys Phe Arg Gln Gln Arg Val Ser Lys Thr Leu Asp Gln  
45 405 410 415

Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His Leu  
420 425 430

50 Asn Gly Arg Asn Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr His  
435 440 445

Lys Asp Asp Glu Glu Arg Phe Ser Pro Ser Ser Gly Val Leu Ile Phe  
55 450 455 460



EP 1 310 571 B1

5 Gly Lys Thr Gly Ala Ala Asn Lys Thr Thr Leu Glu Asn Val Leu Met  
465 470 475 480

Thr Asn Glu Glu Glu Ile Arg Pro Thr Asn Pro Val Ala Thr Glu Glu  
485 490 495

10 Tyr Gly Ile Val Ser Ser Asn Leu Gln Ala Ala Ser Thr Ala Ala Gln  
500 505 510

15 Thr Gln Val Val Asn Asn Gln Gly Ala Leu Pro Gly Met Val Trp Gln  
515 520 525

Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His  
530 535 540

20 Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu  
545 550 555 560

25 Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala  
565 570 575

Asn Pro Pro Glu Val Phe Thr Pro Ala Lys Phe Ala Ser Phe Ile Thr  
580 585 590

30 Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln  
595 600 605

35 Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn  
610 615 620

Phe Asp Lys Gln Thr Gly Val Asp Phe Ala Val Asp Ser Gln Gly Val  
625 630 635 640

40 Tyr Ser Glu Pro

<210> 77

<211> 644

<212> PRT

<213> capsid protein of AAV serotype, clone 223.7

<400> 77

50 Lys Ala Tyr Asp Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg  
1 5 10 15

55 Tyr Asn His Ala Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr  
20 25 30

EP 1 310 571 B1

Ser Phe Gly Gly Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg  
 35 40 45  
 5  
 Val Leu Glu Pro Leu Gly Leu Val Glu Thr Pro Ala Lys Thr Ala Pro  
 50 55 60  
 10  
 Gly Lys Lys Arg Pro Val Asp Ser Pro Asp Ser Thr Ser Gly Ile Gly  
 65 70 75 80  
 Lys Lys Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln Thr  
 85 90 95  
 15  
 Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro Pro  
 100 105 110  
 20  
 Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly Gly  
 115 120 125  
 Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala  
 130 135 140  
 25  
 Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile  
 145 150 155 160  
 30  
 Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu  
 165 170 175  
 Tyr Lys Gln Ile Ser Ser Gln Ser Ala Gly Ser Thr Asn Asp Asn Val  
 180 185 190  
 35  
 Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe  
 195 200 205  
 40  
 His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn  
 210 215 220  
 Trp Gly Phe Arg Pro Lys Lys Leu Asn Phe Lys Leu Phe Asn Ile Gln  
 225 230 235 240  
 45  
 Val Lys Glu Val Thr Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn  
 245 250 255  
 50  
 Leu Thr Ser Thr Val Gln Val Phe Ser Asp Pro Glu Tyr Gln Leu Pro  
 260 265 270  
 Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala  
 275 280 285  
 55

EP 1 310 571 B1

5

Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly  
290 295 300

Ser Gln Ser Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro  
305 310 315 320

10

Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Thr Phe Ser Tyr Thr Phe  
325 330 335

Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp  
340 345 350

15

Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala Arg  
355 360 365

20

Thr Gln Ser Asn Ala Gly Gly Thr Ala Gly Asn Arg Glu Leu Gln Phe  
370 375 380

Tyr Gln Gly Gly Pro Thr Thr Met Ala Glu Gln Ala Lys Asn Trp Leu  
385 390 395 400

25

Pro Gly Pro Cys Phe Arg Gln Gln Arg Val Ser Lys Thr Leu Asp Gln  
405 410 415

30

Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His Leu  
420 425 430

Asn Gly Arg Asn Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr His  
435 440 445

35

Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Ile Phe  
450 455 460

40

Gly Lys Thr Gly Ala Ala Asn Lys Thr Thr Leu Glu Asn Val Leu Met  
465 470 475 480

Thr Asn Glu Glu Glu Ile Arg Pro Thr Asn Pro Val Ala Thr Glu Glu  
485 490 495

45

Tyr Gly Ile Val Ser Ser Asn Leu Gln Ala Ala Ser Thr Ala Ala Gln  
500 505 510

50

Thr Gln Val Val Asn Asn Gln Gly Ala Leu Pro Gly Met Val Trp Gln  
515 520 525

Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His  
530 535 540

55

# EP 1 310 571 B1

Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu  
545 550 555 560

5 Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala  
565 570 575

10 Asn Pro Pro Glu Val Phe Thr Pro Ala Lys Ile Ala Ser Phe Ile Thr  
580 585 590

Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln  
595 600 605

15 Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn  
610 615 620

20 Phe Asp Lys Gln Thr Gly Val Asp Phe Ala Val Asp Ser Gln Gly Val  
625 630 635 640

Tyr Ser Glu Pro

25 <210> 78  
<211> 644  
<212> PRT  
<213> capsid protein of AAV serotype, clone 223.6

30 <400> 78

Lys Ala Tyr Asp Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg  
1 5 10 15

35 Tyr Asn His Ala Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr  
20 25 30

40 Ser Phe Gly Gly Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg  
35 40 45

Val Leu Glu Pro Leu Gly Leu Val Glu Thr Pro Ala Lys Thr Ala Pro  
50 55 60

45 Gly Lys Lys Arg Pro Val Asp Ser Pro Asp Ser Thr Ser Gly Ile Gly  
65 70 75 80

50 Lys Lys Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln Thr  
85 90 95

Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro Pro  
100 105 110

55 Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly Gly  
115 120 125

EP 1 310 571 B1

Ala Pro Met Ala Asp Asn Ser Glu Gly Ala Asp Gly Val Gly Asn Ala  
130 135 140

5

Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile  
145 150 155 160

10

Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu  
165 170 175

Tyr Lys Gln Ile Ser Ser Gln Ser Ala Gly Ser Thr Asn Asp Asn Val  
180 185 190

15

Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe  
195 200 205

20

His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn  
210 215 220

Trp Gly Phe Arg Pro Lys Lys Leu Asn Phe Lys Leu Phe Asn Ile Gln  
225 230 235 240

25

Val Lys Glu Val Thr Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn  
245 250 255

30

Leu Thr Ser Thr Val Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro  
260 265 270

Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala  
275 280 285

35

Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly  
290 295 300

40

Ser Gln Ser Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro  
305 310 315 320

Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Thr Phe Ser Tyr Thr Phe  
325 330 335

45

Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp  
340 345 350

50

Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala Arg  
355 360 365

Thr Gln Ser Asn Ala Gly Gly Thr Ala Gly Asn Arg Glu Leu Gln Phe  
370 375 380

55

EP 1 310 571 B1

Tyr Gln Gly Gly Pro Thr Thr Met Ala Glu Gln Ala Lys Asn Trp Leu  
 385 390 395 400  
 5 Pro Gly Pro Cys Phe Arg Gln Gln Arg Val Ser Lys Thr Leu Asp Gln  
 405 410 415  
 10 Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His Leu  
 420 425 430  
 Asn Gly Arg Asn Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr His  
 435 440 445  
 15 Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Ile Phe  
 450 455 460  
 20 Gly Lys Thr Gly Ala Ala Asn Lys Thr Thr Leu Glu Asn Val Leu Met  
 465 470 475 480  
 Thr Asn Glu Glu Glu Ile Arg Pro Thr Asn Pro Val Ala Thr Glu Glu  
 485 490 495  
 25 Tyr Gly Ile Val Ser Ser Asn Leu Gln Ala Ala Ser Thr Ala Ala Gln  
 500 505 510  
 30 Thr Gln Val Val Asn Asn Gln Gly Ala Leu Pro Gly Met Val Trp Gln  
 515 520 525  
 Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His  
 530 535 540  
 35 Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu  
 545 550 555 560  
 40 Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala  
 565 570 575  
 Asn Pro Pro Glu Val Phe Thr Pro Ala Lys Leu Ala Ser Phe Ile Thr  
 580 585 590  
 45 Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln  
 595 600 605  
 50 Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn  
 610 615 620  
 Phe Asp Lys Gln Thr Gly Val Asp Phe Ala Val Asp Ser Gln Gly Val  
 625 630 635 640

Tyr Ser Glu Pro

5

&lt;210&gt; 79

&lt;211&gt; 738

&lt;212&gt; PRT

10 &lt;213&gt; capsid protein of AAV serotype, clone 44.1

&lt;400&gt; 79

15

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
1 5 10 15Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
20 25 30

20

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
35 40 45

25

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

30

Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
85 90 95

35

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
100 105 110Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
115 120 125

40

Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
130 135 140

45

Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile  
145 150 155 160Gly Lys Lys Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln  
165 170 175

50

Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro  
180 185 190

55

Pro Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly  
195 200 205

EP 1 310 571 B1

Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser  
 210 215 220  
 5  
 Ser Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val  
 225 230 235 240  
 10  
 Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His  
 245 250 255  
 Leu Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp  
 260 265 270  
 15  
 Asn Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn  
 275 280 285  
 20  
 Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn  
 290 295 300  
 Asn Asn Trp Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn  
 305 310 315 320  
 25  
 Ile Gln Val Lys Glu Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala  
 325 330 335  
 30  
 Asn Asn Leu Thr Ser Thr Ile Gln Val Phe Thr Asp Ser Glu Tyr Gln  
 340 345 350  
 Leu Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe  
 355 360 365  
 35  
 Pro Ala Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn  
 370 375 380  
 40  
 Asn Gly Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr  
 385 390 395 400  
 Phe Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr  
 405 410 415  
 45  
 Gln Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser  
 420 425 430  
 50  
 Leu Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu  
 435 440 445  
 Ser Arg Thr Gln Ser Thr Gly Gly Thr Ala Gly Thr Gln Gln Leu Leu  
 450 455 460  
 55



EP 1 310 571 B1

Phe Ser Gln Ala Gly Pro Asn Asn Met Ser Ala Gln Ala Lys Asn Trp  
 465 470 475 480  
 5  
 Leu Pro Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Thr Thr Leu Ser  
 485 490 495  
 10  
 Gln Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His  
 500 505 510  
 Leu Asn Gly Arg Asp Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr  
 515 520 525  
 15  
 His Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Met  
 530 535 540  
 20  
 Phe Gly Lys Gln Gly Ala Gly Lys Asp Asn Val Asp Tyr Ser Ser Val  
 545 550 555 560  
 Met Leu Thr Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr  
 565 570 575  
 25  
 Glu Gln Tyr Gly Val Val Ala Asp Asn Leu Gln Gln Gln Asn Ala Ala  
 580 585 590  
 30  
 Pro Ile Val Gly Ala Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val  
 595 600 605  
 Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile  
 610 615 620  
 35  
 Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe  
 625 630 635 640  
 40  
 Gly Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val  
 645 650 655  
 Pro Ala Asp Pro Pro Thr Thr Phe Ser Gln Ala Lys Leu Ala Ser Phe  
 660 665 670  
 45  
 Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu  
 675 680 685  
 50  
 Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr  
 690 695 700  
 Ser Asn Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Asp  
 705 710 715 720  
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EP 1 310 571 B1

Gly Thr Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg  
725 730 735

5

Asn Leu

10

<210> 80

<211> 738

<212> PRT

<213> capsid protein of AAV serotype, clone 44.5

15

<400> 80

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50

55

EP 1 310 571 B1

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
1 5 10 15

5 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
20 25 30

10 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60

15 Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

20 Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
100 105 110

25 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
115 120 125

30 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
130 135 140

Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile  
145 150 155 160

35 Gly Lys Lys Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln  
165 170 175

40 Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro  
180 185 190

Pro Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly  
195 200 205

45

50

55

EP 1 310 571 B1

Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser  
 210 215 220  
 5  
 Ser Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val  
 225 230 235 240  
 10  
 Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His  
 245 250 255  
 Leu Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp  
 260 265 270  
 15  
 Asn Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn  
 275 280 285  
 20  
 Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn  
 290 295 300  
 Asn Asn Trp Gly Phe Arg Pro Lys Arg Pro Asn Phe Lys Leu Phe Asn  
 305 310 315 320  
 25  
 Ile Gln Val Lys Glu Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala  
 325 330 335  
 30  
 Asn Asn Leu Thr Ser Thr Ile Gln Val Phe Thr Asp Ser Glu Tyr Gln  
 340 345 350  
 Leu Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe  
 355 360 365  
 35  
 Pro Ala Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn  
 370 375 380  
 40  
 Asn Gly Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr  
 385 390 395 400  
 Phe Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr  
 405 410 415  
 45  
 Gln Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser  
 420 425 430  
 50  
 Leu Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu  
 435 440 445  
 Ser Arg Thr Gln Ser Thr Gly Gly Thr Ala Gly Thr Gln Gln Leu Leu  
 450 455 460  
 55

EP 1 310 571 B1

5

Phe Ser Gln Ala Gly Pro Asn Asn Met Ser Ala Gln Ala Lys Asn Trp  
465 470 475 480

Leu Pro Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Thr Thr Leu Ser  
485 490 495

10

Gln Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His  
500 505 510

Leu Asn Gly Arg Asp Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr  
515 520 525

15

His Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Met  
530 535 540

20

Phe Gly Lys Gln Gly Ala Gly Lys Asp Asn Val Asp Tyr Ser Ser Val  
545 550 555 560

Met Leu Thr Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr  
565 570 575

25

Glu Gln Tyr Gly Val Val Ala Asp Asn Leu Gln Gln Gln Asn Ala Ala  
580 585 590

30

Pro Ile Val Gly Ala Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val  
595 600 605

Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile  
610 615 620

35

Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe  
625 630 635 640

40

Gly Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val  
645 650 655

Pro Ala Asp Pro Pro Thr Thr Phe Ser Gln Ala Lys Leu Ala Ser Phe  
660 665 670

45

Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu  
675 680 685

50

Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr  
690 695 700

Ser Asn Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Asp  
705 710 715 720

55

EP 1 310 571 B1

Gly Thr Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg  
725 730 735

5

Asn Leu

10

<210> 81

<211> 738

<212> PRT

<213> capsid protein of AAV serotype, clone 44.2

15

<400> 81

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55

EP 1 310 571 B1

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
1 5 10 15

5 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
20 25 30

10 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60

15 Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

20 Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
100 105 110

25 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
115 120 125

30 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
130 135 140

Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile  
145 150 155 160

35 Gly Lys Lys Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln  
165 170 175

40 Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro  
180 185 190

Pro Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly  
195 200 205

45

50

55

EP 1 310 571 B1

5 Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser  
210 215 220

Ser Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val  
225 230 235 240

10 Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His  
245 250 255

Leu Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp  
260 265 270

15 Asn Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn  
275 280 285

20 Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn  
290 295 300

Asn Asn Trp Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn  
305 310 315 320

25 Ile Gln Val Lys Glu Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala  
325 330 335

30 Asn Asn Leu Thr Ser Thr Ile Gln Val Phe Thr Asp Ser Glu Tyr Gln  
340 345 350

Leu Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe  
355 360 365

35 Pro Ala Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn  
370 375 380

40 Asn Gly Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr  
385 390 395 400

Phe Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr  
405 410 415

45 Gln Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser  
420 425 430

50 Leu Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu  
435 440 445

Ser Arg Thr Gln Ser Thr Gly Gly Thr Ala Gly Thr Gln Gln Leu Leu  
450 455 460



EP 1 310 571 B1

5  
 10  
 15  
 20  
 25  
 30  
 35  
 40  
 45  
 50  
 55

Phe Ser Gln Ala Gly Pro Asn Asn Met Ser Ala Gln Ala Lys Asn Trp  
 465 470 475 480

Leu Pro Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Thr Thr Leu Ser  
 485 490 495

Gln Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His  
 500 505 510

Leu Asn Gly Arg Asp Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr  
 515 520 525

His Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Met  
 530 535 540

Phe Gly Lys Gln Gly Ala Gly Lys Asp Asn Val Asp Tyr Ser Ser Val  
 545 550 555 560

Met Leu Thr Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr  
 565 570 575

Glu Gln Tyr Gly Val Val Ala Asp Asn Leu Gln Gln Gln Asn Ala Ala  
 580 585 590

Pro Ile Val Gly Ala Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val  
 595 600 605

Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile  
 610 615 620

Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe  
 625 630 635 640

Gly Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val  
 645 650 655

Pro Ala Asp Pro Pro Thr Thr Phe Ser Gln Ala Lys Leu Ala Ser Phe  
 660 665 670

Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu  
 675 680 685

Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr  
 690 695 700

Ser Asn Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Asp  
 705 710 715 720

EP 1 310 571 B1

Gly Thr Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg  
725 730 735

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Asn Leu

10

<210> 82

<211> 738

<212> PRT

<213> capsid protein of AAV serotype, clone 29.3VP1

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<400> 82

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EP 1 310 571 B1

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
 1 5 10 15  
 5 Glu Gly Ile Arg Glu Trp Trp Ala Leu Lys Pro Gly Ala Pro Lys Pro  
 20 25 30  
 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
 35 40 45  
 10 Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
 50 55 60  
 Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
 65 70 75 80  
 Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
 85 90 95  
 20 Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
 100 105 110  
 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
 115 120 125  
 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
 130 135 140  
 30 Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Thr Thr Gly Ile  
 145 150 155 160  
 Gly Lys Lys Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln  
 165 170 175  
 35 Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro  
 180 185 190  
 40 Pro Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly  
 195 200 205  
 45  
 50  
 55

EP 1 310 571 B1

5 Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser  
210 215 220

Ser Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val  
225 230 235 240

10 Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His  
245 250 255

Leu Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp  
15 260 265 270

Asn Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn  
275 280 285

20 Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn  
290 295 300

Asn Asn Trp Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn  
25 305 310 315 320

Ile Gln Val Lys Glu Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala  
325 330 335

30 Asn Asn Leu Thr Ser Thr Ile Gln Val Phe Thr Asp Ser Glu Tyr Gln  
340 345 350

Leu Pro Tyr Val Leu Gly Ser Ala Arg Gln Gly Cys Leu Pro Pro Phe  
35 355 360 365

Pro Ala Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn  
370 375 380

40 Asn Gly Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr  
385 390 395 400

Phe Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr  
45 405 410 415

Gln Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser  
420 425 430

50 Leu Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu  
435 440 445

Ser Arg Thr Gln Ser Thr Gly Gly Thr Ala Gly Thr Gln Gln Leu Leu  
55 450 455 460

EP 1 310 571 B1

5 Phe Ser Gln Ala Gly Pro Asn Asn Met Ser Ala Gln Ala Lys Asn Trp  
465 470 475 480

Leu Pro Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Thr Thr Leu Ser  
485 490 495

10 Gln Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His  
500 505 510

15 Leu Asn Gly Arg Asp Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr  
515 520 525

His Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Met  
530 535 540

20 Phe Gly Lys Gln Gly Ala Gly Lys Gly Asn Val Asp Tyr Ser Ser Val  
545 550 555 560

25 Met Leu Thr Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr  
565 570 575

Glu Gln Tyr Gly Val Val Ala Asp Asn Leu Gln Gln Gln Asn Ala Ala  
580 585 590

30 Pro Ile Val Gly Ala Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val  
595 600 605

35 Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile  
610 615 620

Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe  
625 630 635 640

40 Gly Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val  
645 650 655

45 Pro Ala Asp Pro Pro Thr Thr Phe Ser Gln Ala Lys Leu Ala Ser Phe  
660 665 670

Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu  
675 680 685

50 Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr  
690 695 700

55 Ser Asn Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Asp  
705 710 715 720

EP 1 310 571 B1

Gly Thr Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg  
725 730 735

5

Asn Leu

10

<210> 83

<211> 738

<212> PRT

<213> capsid protein of AAV serotype, clone 29.5VP1

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<400> 83

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
1 5 10 15

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Glu Gly Ile Arg Glu Trp Trp Ala Leu Lys Pro Gly Ala Pro Lys Pro  
20 25 30

25

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60

30

Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

35

Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
100 105 110

40

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
115 120 125

45

Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
130 135 140

Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile  
145 150 155 160

50

Gly Lys Lys Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln  
165 170 175

55

Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro  
180 185 190

EP 1 310 571 B1

Pro Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly  
195 200 205

5 Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser  
210 215 220

10 Ser Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Gly Val  
225 230 235 240

Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His  
245 250 255

15 Leu Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp  
260 265 270

20 Asn Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn  
275 280 285

Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn  
290 295 300

25 Asn Asn Trp Gly Phe Arg Pro Lys Ser Leu Asn Phe Lys Leu Phe Asn  
305 310 315 320

30 Ile Gln Val Lys Glu Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala  
325 330 335

Asn Asn Leu Thr Ser Thr Ile Gln Val Phe Thr Asp Ser Glu Tyr Gln  
340 345 350

35 Leu Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe  
355 360 365

40 Pro Ala Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn  
370 375 380

Asn Gly Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr  
385 390 395 400

45 Phe Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr  
405 410 415

50 Gln Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser  
420 425 430

Leu Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu  
435 440 445

55

EP 1 310 571 B1

Ser Arg Thr Gln Ser Thr Gly Gly Thr Ala Gly Thr Gln Gln Leu Leu  
 450 455 460  
 5  
 Phe Ser Gln Ala Gly Pro Asn Asn Met Ser Ala Gln Ala Lys Asn Trp  
 465 470 475 480  
 10  
 Leu Pro Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Thr Thr Leu Ser  
 485 490 495  
 Gln Asn Asp Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His  
 500 505 510  
 15  
 Leu Asn Gly Arg Asp Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr  
 515 520 525  
 His Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Met  
 530 535 540  
 20  
 Phe Gly Lys Gln Gly Ala Gly Lys Asp Asn Val Asp Tyr Ser Ser Val  
 545 550 555 560  
 25  
 Met Leu Thr Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr  
 565 570 575  
 Glu Gln Tyr Gly Val Val Ala Asp Asn Leu Gln Gln Gln Asn Ala Ala  
 580 585 590  
 30  
 Pro Ile Val Gly Ala Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val  
 595 600 605  
 35  
 Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile  
 610 615 620  
 Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe  
 625 630 635 640  
 Gly Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val  
 645 650 655  
 40  
 Pro Ala Asp Pro Pro Thr Thr Phe Ser Gln Ala Lys Leu Ala Ser Phe  
 660 665 670  
 45  
 Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu  
 675 680 685  
 50  
 Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr  
 690 695 700  
 55



EP 1 310 571 B1

Ser Asn Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Asp  
705 710 715 720

5

Gly Thr Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg  
725 730 735

10

Asn Leu

<210> 84

<211> 738

<212> PRT

15

<213> capsid protein of AAV serotype, clone 42.15

<400> 84

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EP 1 310 571 B1

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
1 5 10 15

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
20 25 30

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60

Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
100 105 110

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
115 120 125

Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
130 135 140

Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile  
145 150 155 160

Gly Lys Thr Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln  
165 170 175

Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro  
180 185 190

EP 1 310 571 B1

Pro Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly  
195 200 205

5 Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser  
210 215 220

10 Ser Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val  
225 230 235 240

Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His  
245 250 255

15 Leu Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp  
260 265 270

20 Asn Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn  
275 280 285

Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn  
290 295 300

25 Asn Asn Trp Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn  
305 310 315 320

Ile Gln Val Lys Glu Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala  
325 330 335

30 Asn Asn Leu Thr Ser Thr Ile Gln Val Phe Thr Asp Ser Glu Tyr Gln  
340 345 350

35 Leu Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Pro Pro Pro Phe  
355 360 365

40 Pro Ala Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn  
370 375 380

Asn Gly Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr  
385 390 395 400

45 Phe Pro Ser Gln Met Arg Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr  
405 410 415

Gln Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser  
420 425 430

50 Leu Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu  
435 440 445

55

EP 1 310 571 B1

Ser Arg Thr Gln Ser Thr Gly Gly Thr Ala Gly Thr Gln Gln Leu Leu  
 450 455 460  
 5  
 Phe Ser Gln Ala Gly Pro Asn Asn Met Ser Ala Gln Ala Lys Asn Trp  
 465 470 475 480  
 10  
 Leu Pro Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Thr Thr Leu Ser  
 485 490 495  
 Gln Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His  
 500 505 510  
 15  
 Leu Asn Gly Arg Asp Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr  
 515 520 525  
 His Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Met  
 530 535 540  
 20  
 Phe Gly Lys Gln Gly Ala Gly Lys Asp Asn Val Asp Tyr Ser Ser Val  
 545 550 555 560  
 25  
 Met Leu Thr Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr  
 565 570 575  
 Glu Gln Tyr Gly Val Val Ala Asp Asn Leu Gln Gln Gln Asn Ala Ala  
 580 585 590  
 30  
 Pro Ile Val Gly Ala Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val  
 595 600 605  
 35  
 Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile  
 610 615 620  
 Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe  
 625 630 635 640  
 40  
 Gly Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val  
 645 650 655  
 45  
 Pro Ala Asp Pro Pro Thr Thr Phe Ser Gln Ala Lys Leu Ala Ser Phe  
 660 665 670  
 Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu  
 675 680 685  
 50  
 Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr  
 690 695 700  
 55

# EP 1 310 571 B1

Ser Asn Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu  
 705 710 715 720  
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 Gly Thr Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg  
 725 730 735  
 Asn Leu  
 10  
 <210> 85  
 <211> 738  
 <212> PRT  
 15 <213> capsid protein of AAV serotype, clone 42.8  
 <400> 85  
 20 Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
 1 5 10 15  
 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
 20 25 30  
 25 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
 35 40 45  
 30 Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
 50 55 60  
 Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
 65 70 75 80  
 35 Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
 85 90 95  
 40 Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
 100 105 110  
 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
 115 120 125  
 45 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
 130 135 140  
 50 Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile  
 145 150 155 160  
 Gly Lys Thr Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln  
 165 170 175  
 55

EP 1 310 571 B1

Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro  
 180 185 190  
 5  
 Pro Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly  
 195 200 205  
 10  
 Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser  
 210 215 220  
 Ser Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val  
 225 230 235 240  
 15  
 Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His  
 245 250 255  
 20  
 Leu Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp  
 260 265 270  
 Asn Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn  
 275 280 285  
 25  
 Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn  
 290 295 300  
 30  
 Asn Asn Trp Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn  
 305 310 315 320  
 Ile Gln Val Lys Glu Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala  
 325 330 335  
 35  
 Asn Asn Leu Thr Ser Thr Ile Gln Val Phe Thr Asp Ser Glu Tyr Gln  
 340 345 350  
 40  
 Leu Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe  
 355 360 365  
 Pro Ala Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn  
 370 375 380  
 45  
 Asn Gly Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr  
 385 390 395 400  
 50  
 Phe Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr  
 405 410 415  
 Gln Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser  
 420 425 430  
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EP 1 310 571 B1

5 Leu Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu  
 435 440 445  
 Ser Arg Thr Gln Ser Thr Gly Gly Thr Ala Gly Thr Gln Gln Leu Leu  
 450 455 460  
 10 Phe Ser Gln Ala Gly Pro Asn Asn Met Ser Ala Gln Ala Lys Asn Trp  
 465 470 475 480  
 Leu Pro Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Thr Thr Leu Ser  
 485 490 495  
 15 Gln Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His  
 500 505 510  
 20 Leu Asn Gly Arg Asp Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr  
 515 520 525  
 His Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Met  
 530 535 540  
 25 Phe Gly Lys Gln Gly Ala Gly Lys Asp Asn Val Asp Tyr Ser Ser Val  
 545 550 555 560  
 30 Met Leu Thr Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr  
 565 570 575  
 Glu Gln Tyr Gly Val Val Ala Asp Asn Leu Gln Gln Gln Asn Ala Ala  
 580 585 590  
 35 Pro Ile Val Gly Ala Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val  
 595 600 605  
 40 Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile  
 610 615 620  
 Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe  
 625 630 635 640  
 45 Gly Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val  
 645 650 655  
 50 Pro Ala Asp Pro Pro Thr Thr Phe Ser Gln Ala Lys Leu Ala Ser Phe  
 660 665 670  
 Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu  
 675 680 685

# EP 1 310 571 B1

Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr  
690 695 700

5

Ser Asn Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu  
705 710 715 720

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Gly Thr Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg  
725 730 735

Asn Leu

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<210> 86

<211> 733

<212> PRT

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<213> amino acid of AAV serotype, clone 42.13

<400> 86

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EP 1 310 571 B1

	Met	Ala	Ala	Asp	Gly	Tyr	Leu	Pro	Asp	Trp	Leu	Glu	Asp	Asn	Leu	Ser	
	1				5					10					15		
5	Glu	Gly	Ile	Arg	Glu	Trp	Trp	Asp	Leu	Lys	Pro	Gly	Ala	Pro	Lys	Pro	
				20					25					30			
	Lys	Ala	Asn	Gln	Gln	Lys	Gln	Asp	Asp	Gly	Arg	Gly	Leu	Val	Leu	Pro	
10			35					40					45				
	Gly	Tyr	Lys	Tyr	Leu	Gly	Pro	Phe	Asn	Gly	Leu	Asp	Lys	Gly	Glu	Pro	
		50					55					60					
15	Val	Asn	Ala	Ala	Asp	Ala	Ala	Ala	Leu	Glu	His	Asp	Lys	Ala	Tyr	Asp	
	65					70					75					80	
	Gln	Gln	Leu	Lys	Ala	Gly	Asp	Asn	Pro	Tyr	Leu	Arg	Tyr	Asn	His	Ala	
20					85					90					95		
	Asp	Ala	Glu	Phe	Gln	Glu	Arg	Leu	Gln	Glu	Asp	Thr	Ser	Phe	Gly	Gly	
				100					105					110			
25	Asn	Leu	Gly	Arg	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Val	Leu	Glu	Pro	
			115					120					125				
	Leu	Gly	Leu	Val	Glu	Glu	Gly	Ala	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Arg	
30		130					135					140					
	Pro	Ile	Glu	Ser	Pro	Asp	Ser	Ser	Thr	Gly	Ile	Gly	Lys	Lys	Gly	Gln	
	145					150					155					160	
35	Gln	Pro	Ala	Lys	Lys	Lys	Leu	Asn	Phe	Gly	Gln	Thr	Gly	Asp	Ser	Glu	
					165					170					175		

EP 1 310 571 B1

Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro Pro Ala Gly Pro Ser  
 180 185 190  
 5  
 Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly Gly Ala Pro Met Ala  
 195 200 205  
 Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser Ser Ser Gly Asn Trp  
 210 215 220  
 10  
 His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile Thr Thr Ser Thr  
 225 230 235 240  
 Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu Tyr Lys Gln Ile  
 245 250 255  
 15  
 Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp Asn Thr Tyr Phe Gly  
 260 265 270  
 20  
 Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His Cys His  
 275 280 285  
 25  
 Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp Gly Phe  
 290 295 300  
 Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn Ile Gln Val Lys Glu  
 305 310 315 320  
 30  
 Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala Asn Asn Leu Thr Ser  
 325 330 335  
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 Thr Ile Gln Val Phe Thr Asp Ser Glu Tyr Gln Leu Pro Tyr Val Leu  
 340 345 350  
 Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp Val Phe  
 355 360 365  
 40  
 Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser Gln Ala  
 370 375 380  
 45  
 Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met  
 385 390 395 400  
 Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr Gln Phe Glu Asp Val  
 405 410 415  
 50  
 Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg Leu Met  
 420 425 430  
 55

EP 1 310 571 B1

5

Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ser Arg Thr Gln Ser  
435 440 445

Thr Gly Gly Thr Ala Gly Thr Gln Gln Leu Leu Phe Ser Gln Ala Gly  
450 455 460

10

Pro Asn Asn Met Ser Ala Gln Ala Lys Asn Trp Leu Pro Gly Pro Cys  
465 470 475 480

Tyr Arg Gln Gln Arg Val Ser Thr Thr Val Ser Gln Asn Asn Asn Ser  
485 490 495

15

Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His Leu Asn Gly Arg Asp  
500 505 510

20

Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr His Lys Gly Asp Glu  
515 520 525

Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Met Phe Gly Lys Gln Gly  
530 535 540

25

Ala Gly Lys Asp Asn Val Asp Tyr Ser Ser Val Met Leu Thr Ser Glu  
545 550 555 560

30

Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr Glu Gln Tyr Gly Val  
565 570 575

Val Ala Asp Asn Leu Gln Gln Gln Asn Ala Ala Pro Ile Val Gly Ala  
580 585 590

35

Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val Trp Gln Asn Arg Asp  
595 600 605

40

Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His Thr Asp Gly  
610 615 620

Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu Lys His Pro  
625 630 635 640

45

Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala Asp Pro Pro  
645 650 655

50

Thr Thr Phe Ser Gln Ala Lys Leu Ala Ser Phe Ile Thr Gln Tyr Ser  
660 665 670

Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln Lys Glu Asn  
675 680 685

55

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Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn Tyr Tyr Lys  
690 695 700

5

Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu Gly Thr Tyr Ser Glu  
705 710 715 720

10

Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Ser Leu  
725 730

15

<210> 87

<211> 733

<212> PRT

<213> capsid protein of AAV serotype, clone 42.3A

<400> 87

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25

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45

50

55

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	Met	Ala	Ala	Asp	Gly	His	Leu	Pro	Asp	Trp	Leu	Glu	Asp	Asn	Leu	Ser	
	1				5					10					15		
5	Glu	Gly	Ile	Arg	Glu	Trp	Trp	Asp	Leu	Lys	Pro	Gly	Ala	Pro	Lys	Pro	
				20					25					30			
	Lys	Ala	Asn	Gln	Gln	Lys	Gln	Asp	Asp	Gly	Arg	Gly	Leu	Val	Leu	Pro	
10			35					40					45				
	Gly	Tyr	Lys	Tyr	Leu	Gly	Pro	Phe	Asn	Gly	Leu	Asp	Lys	Gly	Glu	Pro	
		50					55					60					
15	Val	Asn	Ala	Ala	Asp	Ala	Ala	Ala	Leu	Glu	His	Asp	Lys	Ala	Tyr	Asp	
	65					70					75					80	
	Gln	Gln	Leu	Lys	Ala	Gly	Asp	Asn	Pro	Tyr	Leu	Arg	Tyr	Asn	His	Ala	
20				85						90					95		
	Asp	Ala	Glu	Phe	Gln	Glu	Arg	Leu	Gln	Glu	Asp	Thr	Ser	Phe	Gly	Gly	
				100					105					110			
25	Asn	Leu	Gly	Arg	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Val	Leu	Glu	Pro	
			115					120					125				
	Leu	Gly	Leu	Val	Glu	Glu	Gly	Ala	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Arg	
30		130					135					140					
	Pro	Ile	Glu	Ser	Pro	Asp	Ser	Ser	Thr	Gly	Ile	Gly	Lys	Lys	Gly	Gln	
	145					150					155					160	
35	Gln	Pro	Ala	Lys	Lys	Lys	Leu	Asn	Phe	Gly	Gln	Thr	Gly	Asp	Ser	Glu	
				165						170					175		
	Ser	Val	Pro	Asp	Pro	Gln	Pro	Ile	Gly	Glu	Pro	Pro	Ala	Gly	Pro	Ser	
40				180					185					190			

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5 Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly Gly Ala Pro Met Ala  
195 200 205

Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser Ser Ser Gly Asn Trp  
210 215 220

10 His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile Thr Thr Ser Thr  
225 230 235 240

Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu Tyr Lys Gln Ile  
245 250 255

15 Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp Asn Thr Tyr Phe Gly  
260 265 270

20 Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His Cys His  
275 280 285

Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Ser Trp Gly Phe  
290 295 300

25 Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn Ile Gln Val Lys Glu  
305 310 315 320

30 Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala Asn Asn Leu Thr Ser  
325 330 335

Thr Ile Gln Val Phe Thr Asp Ser Glu Tyr Gln Leu Pro Tyr Val Leu  
340 345 350

35 Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp Val Phe  
355 360 365

40 Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser Gln Ala  
370 375 380

Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met  
385 390 395 400

45 Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr Gln Phe Glu Asp Val  
405 410 415

50 Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg Leu Met  
420 425 430

Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ser Arg Thr Gln Ser  
435 440 445

55

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5  
 Thr Gly Gly Thr Ala Gly Thr Gln Gln Leu Leu Phe Ser Gln Ala Gly  
 450 455 460

10  
 Pro Asn Asn Met Ser Ala Gln Ala Lys Asn Trp Leu Pro Gly Pro Cys  
 465 470 475 480

15  
 Tyr Arg Gln Gln Arg Val Ser Thr Thr Leu Ser Gln Asn Asn Asn Ser  
 485 490 495

20  
 Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His Leu Asn Gly Arg Asp  
 500 505 510

25  
 Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr His Lys Asp Asp Glu  
 515 520 525

30  
 Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Met Phe Gly Lys Gln Gly  
 530 535 540

35  
 Ala Gly Lys Asp Asn Val Asp Tyr Ser Ser Val Met Leu Thr Ser Glu  
 545 550 555 560

40  
 Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr Glu Gln Tyr Gly Val  
 565 570 575

45  
 Val Ala Asp Asn Leu Gln Gln Gln Asn Ala Ala Pro Ile Val Gly Ala  
 580 585 590

50  
 Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val Trp Gln Asn Arg Asp  
 595 600 605

55  
 Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His Thr Asp Gly  
 610 615 620

60  
 Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu Lys His Pro  
 625 630 635 640

65  
 Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala Asp Pro Pro  
 645 650 655

70  
 Thr Thr Phe Ser Gln Ala Lys Leu Ala Ser Phe Ile Thr Gln Tyr Ser  
 660 665 670

75  
 Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln Lys Glu Asn  
 675 680 685

80  
 Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn Tyr Tyr Lys  
 690 695 700

# EP 1 310 571 B1

Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu Gly Thr Tyr Ser Glu  
705 710 715 720

5

Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu  
725 730

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<210> 88  
<211> 731  
<212> PRT  
<213> capsid protein of AAV serotype, clone 42.4

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<400> 88

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
1 5 10 15

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Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
20 25 30

25

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60

30

Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

35

Lys Gln Leu Glu Gln Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala  
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
100 105 110

40

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
115 120 125

45

Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
130 135 140

Pro Ile Glu Ser Pro Asp Ser Ser Thr Gly Ile Gly Lys Lys Gly Gln  
145 150 155 160

50

Gln Pro Ala Lys Lys Lys Leu Asn Phe Gly Gln Thr Gly Asp Ser Glu  
165 170 175

55

Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro Pro Ala Gly Pro Ser  
180 185 190



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Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly Gly Ala Pro Met Ala  
 195 200 205  
 5  
 Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala Ser Gly Asn Trp  
 210 215 220  
 10  
 His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile Thr Thr Ser Thr  
 225 230 235 240  
 Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu Tyr Lys Gln Ile  
 245 250 255  
 15  
 Ser Ser Gln Ser Gly Ala Thr Asn Asp Asn His Phe Phe Gly Tyr Ser  
 260 265 270  
 20  
 Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His Cys His Phe Ser  
 275 280 285  
 Ser Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp Gly Phe Arg Pro  
 290 295 300  
 25  
 Lys Arg Leu Asn Phe Lys Leu Phe Asn Ile Gln Val Lys Glu Val Thr  
 305 310 315 320  
 30  
 Gln Asn Glu Gly Thr Lys Thr Ile Ala Asn Asn Leu Thr Ser Thr Ile  
 325 330 335  
 Gln Val Phe Thr Asp Ser Glu Tyr Arg Leu Pro Tyr Val Leu Gly Ser  
 340 345 350  
 35  
 Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp Val Phe Met Ile  
 355 360 365  
 40  
 Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser Gln Ala Val Gly  
 370 375 380  
 Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met Leu Arg  
 385 390 395 400  
 45  
 Thr Gly Asn Asn Phe Glu Phe Ser Tyr Gln Phe Glu Asp Val Pro Phe  
 405 410 415  
 50  
 His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg Leu Met Asn Pro  
 420 425 430  
 Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ser Arg Thr Gln Ser Thr Gly  
 435 440 445  
 55

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5 Gly Thr Ala Gly Thr Gln Gln Leu Leu Phe Ser Gln Ala Gly Pro Asn  
450 455 460

Asn Met Ser Ala Gln Ala Lys Asn Trp Leu Pro Gly Pro Cys Tyr Arg  
465 470 475 480

10 Gln Gln Arg Val Ser Thr Thr Leu Ser Gln Asn Asn Asn Ser Asn Phe  
485 490 495

Ala Trp Thr Gly Ala Thr Lys Tyr His Leu Asn Gly Arg Asp Ser Leu  
500 505 510

15 Val Asn Pro Gly Val Ala Met Ala Thr His Lys Asp Asp Glu Glu Arg  
515 520 525

20 Phe Phe Pro Ser Ser Gly Val Leu Met Phe Gly Lys Gln Gly Ala Gly  
530 535 540

25 Lys Asp Asn Val Asp Tyr Ser Ser Val Met Leu Thr Ser Glu Glu Glu  
545 550 555 560

Ile Lys Thr Thr Asn Pro Val Ala Thr Glu Gln Tyr Gly Val Val Ala  
565 570 575

30 Asp Asn Leu Gln Gln Gln Asn Ala Ala Pro Ile Val Gly Ala Val Asn  
580 585 590

35 Ser Gln Gly Ala Leu Pro Gly Met Val Trp Gln Asn Arg Asp Val Tyr  
595 600 605

Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His Thr Asp Gly Asn Phe  
610 615 620

40 His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu Lys His Pro Pro Pro  
625 630 635 640

45 Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala Asp Pro Pro Thr Thr  
645 650 655

Phe Ser Gln Ala Lys Pro Ala Ser Phe Ile Thr Gln Tyr Ser Thr Gly  
660 665 670

50 Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln Lys Glu Asn Ser Lys  
675 680 685

55 Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn Tyr Tyr Lys Ser Thr  
690 695 700

EP 1 310 571 B1

Asn Val Asp Phe Ala Val Asn Thr Glu Gly Thr Tyr Ser Glu Pro Arg  
705 710 715 720

5

Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu  
725 730

10

<210> 89  
<211> 731  
<212> PRT  
<213> capsid protein of AAV serotype, clone 42.5A

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<400> 89

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50

55

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	Met	Ala	Ala	Asp	Gly	Tyr	Leu	Pro	Asp	Trp	Leu	Glu	Asp	Asn	Leu	Ser	
	1				5					10					15		
5	Glu	Gly	Ile	Arg	Glu	Trp	Trp	Asp	Leu	Lys	Pro	Gly	Ala	Pro	Lys	Pro	
				20					25					30			
	Lys	Ala	Asn	Gln	Gln	Lys	Gln	Asp	Asp	Gly	Arg	Gly	Leu	Val	Leu	Pro	
			35					40					45				
10	Gly	Tyr	Lys	Tyr	Leu	Gly	Pro	Phe	Asn	Gly	Leu	Asp	Lys	Gly	Glu	Pro	
		50					55					60					
	Val	Asn	Glu	Ala	Asp	Ala	Ala	Ala	Leu	Glu	His	Asp	Lys	Ala	Tyr	Asp	
15		65				70					75					80	
	Lys	Gln	Leu	Glu	Gln	Gly	Asp	Asn	Pro	Tyr	Leu	Lys	Tyr	Asn	His	Ala	
					85					90					95		
20	Asp	Ala	Glu	Phe	Gln	Glu	Arg	Leu	Gln	Glu	Asp	Thr	Ser	Phe	Gly	Gly	
				100					105					110			
	Asn	Leu	Gly	Arg	Ala	Val	Phe	Arg	Ala	Lys	Lys	Arg	Val	Leu	Glu	Pro	
25			115					120					125				
	Leu	Gly	Leu	Val	Glu	Glu	Gly	Ala	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Arg	
		130					135					140					
30	Pro	Ile	Glu	Ser	Pro	Asp	Ser	Ser	Thr	Gly	Ile	Gly	Lys	Lys	Gly	Gln	
		145				150					155					160	
	Gln	Pro	Ala	Lys	Lys	Lys	Leu	Asn	Phe	Gly	Gln	Thr	Gly	Asp	Ser	Glu	
35					165					170					175		
	Ser	Val	Pro	Asp	Pro	Gln	Pro	Leu	Gly	Glu	Pro	Pro	Ala	Ala	Pro	Ser	
				180					185					190			
40	Gly	Leu	Gly	Ser	Gly	Thr	Met	Ala	Ala	Gly	Gly	Gly	Ala	Pro	Met	Ala	
			195					200					205				

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5 Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala Ser Gly Asn Trp  
210 215 220

10 His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile Thr Thr Ser Thr  
225 230 235 240

15 Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu Tyr Lys Gln Ile  
245 250 255

20 Ser Ser Gln Ser Gly Ala Thr Asn Asp Asn His Phe Phe Gly Tyr Ser  
260 265 270

25 Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His Cys His Phe Ser  
275 280 285

30 Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Arg Gly Phe Arg Pro  
290 295 300

35 Arg Lys Leu Arg Phe Lys Leu Phe Asn Ile Gln Val Lys Glu Val Thr  
305 310 315 320

40 Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn Leu Thr Ser Thr Ile  
325 330 335

45 Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro Tyr Val Leu Gly Ser  
340 345 350

50 Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp Val Phe Met Ile  
355 360 365

55 Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser Gln Ser Val Gly  
370 375 380

Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met Leu Arg  
385 390 395 400

Thr Gly Asn Asn Phe Glu Phe Ser Tyr Gln Phe Glu Asp Val Pro Phe  
405 410 415

His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg Leu Met Asn Pro  
420 425 430

Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ser Arg Thr Gln Ser Thr Gly  
435 440 445

Gly Thr Ala Gly Thr Gln Gln Leu Leu Phe Ser Gln Ala Gly Pro Asn  
450 455 460

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	Asn	Met	Ser	Ala	Gln	Ala	Lys	Asn	Trp	Leu	Pro	Gly	Pro	Cys	Tyr	Arg
	465					470					475					480
5	Gln	Gln	Arg	Val	Ser	Thr	Thr	Leu	Ser	Gln	Asn	Asn	Asn	Ser	Asn	Phe
					485					490					495	
10	Ala	Trp	Thr	Gly	Ala	Thr	Lys	Tyr	His	Leu	Asn	Gly	Arg	Asp	Ser	Leu
				500					505					510		
15	Val	Asn	Pro	Gly	Val	Ala	Met	Ala	Thr	His	Lys	Asp	Asp	Glu	Glu	Arg
			515					520					525			
20	Phe	Phe	Pro	Ser	Ser	Gly	Val	Leu	Met	Phe	Gly	Lys	Gln	Gly	Ala	Gly
	530						535					540				
25	Lys	Asp	Asn	Val	Asp	Tyr	Ser	Ser	Val	Met	Leu	Thr	Ser	Glu	Glu	Glu
	545					550					555					560
30	Ile	Lys	Thr	Thr	Asn	Pro	Val	Ala	Thr	Glu	Gln	Tyr	Gly	Val	Val	Ala
					565					570					575	
35	Asp	Asn	Leu	Gln	Gln	Gln	Asn	Ala	Ala	Pro	Ile	Val	Gly	Ala	Val	Asn
				580					585					590		
40	Ser	Gln	Gly	Ala	Leu	Pro	Gly	Met	Ala	Trp	Gln	Asn	Arg	Asp	Val	Tyr
			595					600					605			
45	Leu	Gln	Gly	Pro	Ile	Trp	Ala	Lys	Ile	Pro	His	Thr	Asp	Gly	Asn	Phe
	610						615					620				
50	His	Pro	Ser	Pro	Leu	Met	Gly	Gly	Phe	Gly	Leu	Lys	His	Pro	Pro	Pro
	625					630					635					640
55	Gln	Ile	Leu	Ile	Lys	Asn	Thr	Pro	Val	Pro	Ala	Asp	Pro	Pro	Thr	Thr
					645					650					655	
60	Phe	Ser	Gln	Ala	Lys	Leu	Ala	Ser	Phe	Ile	Thr	Gln	Tyr	Ser	Thr	Gly
				660					665					670		
65	Gln	Val	Ser	Val	Glu	Ile	Glu	Trp	Glu	Leu	Gln	Lys	Glu	Asn	Ser	Lys
			675					680					685			
70	Arg	Trp	Asn	Pro	Glu	Ile	Gln	Tyr	Thr	Ser	Asn	Tyr	Tyr	Lys	Ser	Thr
	690						695					700				
75	Asn	Val	Asp	Phe	Ala	Val	Asn	Thr	Glu	Gly	Thr	Tyr	Ser	Glu	Pro	Arg
	705					710					715					720

# EP 1 310 571 B1

Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu  
725 730

5

<210> 90

<211> 733

<212> PRT

<213> capsid protein of AAV serotype, clone 42.1B

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<400> 90

15

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
1 5 10 15

Glu Gly Ile Arg Glu Trp Trp Asp Leu Arg Pro Gly Ala Pro Lys Pro  
20 25 30

20

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
35 40 45

25

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60

Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

30

Lys Gln Leu Glu Gln Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala  
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
100 105 110

35

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
115 120 125

40

Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
130 135 140

Pro Ile Glu Ser Pro Asp Ser Ser Thr Gly Ile Gly Lys Lys Gly Gln  
145 150 155 160

45

Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln Thr Gly Asp Ser Glu  
165 170 175

50

Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro Pro Ala Gly Pro Ser  
180 185 190

Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly Gly Ala Pro Met Ala  
195 200 205

55

Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser Ser Ser Gly Asn Trp  
210 215 220

EP 1 310 571 B1

5 His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile Thr Thr Ser Thr  
 225 230 235 240  
 Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu Tyr Lys Gln Ile  
 245 250 255  
 10 Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp Asn Thr Tyr Phe Gly  
 260 265 270  
 Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His Cys His  
 275 280 285  
 15 Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp Gly Phe  
 290 295 300  
 20 Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn Ile Gln Val Lys Glu  
 305 310 315 320  
 Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala Asn Asn Leu Thr Ser  
 325 330 335  
 25 Thr Ile Gln Val Phe Thr Asp Ser Glu Tyr Gln Leu Pro Tyr Val Leu  
 340 345 350  
 Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp Val Phe  
 355 360 365  
 30 Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser Gln Ala  
 370 375 380  
 35 Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met  
 385 390 395 400  
 Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr Gln Phe Glu Asp Val  
 405 410 415  
 40 Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg Leu Met  
 420 425 430  
 45 Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ser Arg Thr Gln Ser  
 435 440 445  
 Thr Gly Gly Thr Ala Gly Thr Gln Gln Leu Leu Phe Ser Gln Ala Gly  
 450 455 460  
 50 Pro Asn Asn Met Ser Ala Gln Ala Lys Asn Trp Leu Pro Gly Pro Cys  
 465 470 475 480  
 55



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5 Tyr Arg Gln Gln Arg Val Ser Thr Thr Val Ser Gln Asn Asn Asn Ser  
485 490 495

Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His Leu Asn Gly Arg Asp  
500 505 510

10 Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr His Lys Gly Asp Glu  
515 520 525

Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Met Phe Gly Lys Gln Gly  
530 535 540

15 Ala Gly Lys Asp Asn Val Asp Tyr Ser Ser Val Met Leu Thr Ser Glu  
545 550 555 560

20 Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr Glu Gln Tyr Gly Val  
565 570 575

Val Ala Asp Asn Leu Gln Gln Gln Asn Ala Ala Pro Ile Val Gly Ala  
580 585 590

25 Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val Trp Gln Asn Arg Asp  
595 600 605

30 Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His Thr Asp Gly  
610 615 620

Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu Lys His Pro  
625 630 635 640

35 Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala Asp Pro Pro  
645 650 655

40 Thr Thr Phe Ser Gln Ala Lys Leu Ala Ser Phe Ile Thr Gln Tyr Ser  
660 665 670

Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln Lys Glu Asn  
675 680 685

45 Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn Tyr Tyr Lys  
690 695 700

50 Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu Gly Thr Tyr Ser Glu  
705 710 715 720

Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu  
725 730

<210> 91

# EP 1 310 571 B1

<211> 738

<212> PRT

<213> capsid protein of AAV serotype, clone 42.5B

5 <400> 91

	Met	Ala	Ala	Asp	Gly	Tyr	Leu	Pro	Asp	Trp	Leu	Glu	Asp	Asn	Leu	Ser	
	1				5					10					15		
10	Glu	Gly	Ile	Arg	Glu	Trp	Trp	Asp	Leu	Lys	Pro	Gly	Ala	Pro	Lys	Pro	
				20					25					30			
	Lys	Ala	Asn	Gln	Gln	Lys	Gln	Asp	Asp	Gly	Arg	Gly	Leu	Val	Leu	Pro	
			35					40					45				
15	Gly	Tyr	Lys	Tyr	Leu	Gly	Pro	Phe	Asn	Gly	Leu	Asp	Lys	Gly	Glu	Pro	
		50					55					60					
	Val	Asn	Glu	Ala	Asp	Ala	Ala	Ala	Leu	Glu	His	Asp	Lys	Ala	Tyr	Asp	
	65					70					75					80	
20	Lys	Gln	Leu	Glu	Gln	Gly	Asp	Asn	Pro	Tyr	Leu	Lys	Tyr	Asn	His	Ala	
					85					90					95		
25	Asp	Ala	Glu	Phe	Gln	Glu	Arg	Leu	Gln	Glu	Asp	Thr	Ser	Phe	Gly	Gly	
				100					105					110			
	Asn	Leu	Gly	Arg	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Val	Leu	Glu	Pro	
			115					120					125				
30	Leu	Gly	Leu	Val	Glu	Glu	Gly	Ala	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Arg	
		130					135					140					
35	Pro	Val	Glu	Pro	Ser	Pro	Gln	Arg	Ser	Pro	Asp	Ser	Ser	Thr	Gly	Ile	
	145					150					155					160	
	Gly	Lys	Thr	Gly	Gln	Gln	Pro	Ala	Lys	Lys	Arg	Leu	Asn	Phe	Gly	Gln	
					165					170					175		
40	Thr	Gly	Asp	Ser	Glu	Ser	Val	Pro	Asp	Pro	Gln	Pro	Ile	Gly	Glu	Pro	
				180					185					190			
45	Pro	Ala	Gly	Pro	Ser	Gly	Leu	Gly	Ser	Gly	Thr	Met	Ala	Ala	Gly	Gly	
			195					200					205				
	Gly	Ala	Pro	Met	Ala	Asp	Asn	Asn	Glu	Gly	Ala	Asp	Gly	Val	Gly	Ser	
		210					215					220					
50	Ser	Ser	Gly	Asn	Trp	His	Cys	Asp	Ser	Thr	Trp	Leu	Gly	Asp	Arg	Val	
	225					230					235					240	
55	Ile	Thr	Thr	Ser	Thr	Arg	Thr	Trp	Ala	Leu	Pro	Thr	Tyr	Asn	Asn	His	
					245					250					255		

EP 1 310 571 B1

5 Leu Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp  
 260 265 270  
 Asn Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn  
 275 280 285  
 10 Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn  
 290 295 300  
 Asn Asn Trp Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn  
 305 310 315 320  
 15 Ile Gln Val Lys Glu Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala  
 325 330 335  
 Asn Asn Leu Thr Ser Thr Ile Gln Val Phe Thr Asp Ser Glu Tyr Gln  
 340 345 350  
 20 Leu Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe  
 355 360 365  
 25 Pro Ala Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn  
 370 375 380  
 Asn Gly Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr  
 385 390 395 400  
 30 Phe Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr  
 405 410 415  
 35 Gln Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser  
 420 425 430  
 Leu Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu  
 435 440 445  
 40 Ser Arg Thr Gln Ser Thr Gly Gly Thr Ala Gly Thr Gln Gln Leu Leu  
 450 455 460  
 45 Phe Ser Gln Ala Gly Pro Asn Asn Met Ser Ala Gln Ala Lys Asn Trp  
 465 470 475 480  
 Leu Pro Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Thr Thr Leu Ser  
 485 490 495  
 50 Gln Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His  
 500 505 510

55

EP 1 310 571 B1

Leu Asn Gly Arg Asp Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr  
 515 520 525  
 5  
 His Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Met  
 530 535 540  
 10  
 Phe Gly Lys Gln Gly Ala Gly Lys Asp Asn Val Asp Tyr Ser Ser Val  
 545 550 555 560  
 Met Leu Thr Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr  
 565 570 575  
 15  
 Glu Gln Tyr Gly Val Val Ala Asp Asn Leu Gln Gln Gln Asn Ala Ala  
 580 585 590  
 Pro Ile Val Gly Ala Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val  
 595 600 605  
 20  
 Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile  
 610 615 620  
 25  
 Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe  
 625 630 635 640  
 Gly Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val  
 645 650 655  
 30  
 Pro Ala Asp Pro Pro Thr Thr Phe Ser Gln Ala Lys Leu Ala Ser Phe  
 660 665 670  
 35  
 Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu  
 675 680 685  
 Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr  
 690 695 700  
 40  
 Ser Asn Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu  
 705 710 715 720  
 45  
 Gly Thr Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg  
 725 730 735  
 Asn Leu  
 50  
 <210> 92  
 <211> 738  
 <212> PRT  
 <213> capsid protein of AAV serotype, clone 43.1  
 55  
 <400> 92

EP 1 310 571 B1

	Met	Ala	Ala	Asp	Gly	Tyr	Leu	Pro	Asp	Trp	Leu	Glu	Asp	Asn	Leu	Ser	
	1				5					10					15		
5	Glu	Gly	Ile	Arg	Glu	Trp	Trp	Asp	Leu	Lys	Pro	Gly	Ala	Pro	Lys	Pro	
				20					25					30			
	Lys	Ala	Asn	Gln	Gln	Lys	Gln	Asp	Asp	Gly	Arg	Gly	Leu	Val	Leu	Pro	
			35					40					45				
10	Gly	Tyr	Lys	Tyr	Leu	Gly	Pro	Phe	Asn	Gly	Leu	Asp	Lys	Gly	Glu	Pro	
		50					55					60					
	Val	Asn	Ala	Ala	Asp	Ala	Ala	Ala	Leu	Glu	His	Asp	Lys	Ala	Tyr	Asp	
15	65					70					75					80	
	Gln	Gln	Leu	Lys	Ala	Gly	Asp	Asn	Pro	Tyr	Leu	Arg	Tyr	Asn	His	Ala	
					85					90					95		
20	Asp	Ala	Glu	Phe	Gln	Glu	Arg	Leu	Gln	Glu	Asp	Thr	Ser	Phe	Gly	Gly	
				100					105						110		
	Asn	Leu	Gly	Arg	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Val	Leu	Glu	Pro	
25			115					120					125				
	Leu	Gly	Leu	Val	Glu	Glu	Gly	Ala	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Arg	
		130					135					140					
30	Pro	Val	Glu	Pro	Ser	Pro	Gln	Arg	Ser	Pro	Asp	Ser	Ser	Thr	Gly	Ile	
	145					150					155					160	
	Gly	Lys	Lys	Gly	His	Gln	Pro	Ala	Arg	Lys	Arg	Leu	Asn	Phe	Gly	Gln	
35					165					170					175		
	Thr	Gly	Asp	Ser	Glu	Ser	Val	Pro	Asp	Pro	Gln	Pro	Ile	Gly	Glu	Pro	
				180					185					190			
40	Pro	Ala	Gly	Pro	Ser	Gly	Leu	Gly	Ser	Gly	Thr	Met	Ala	Ala	Gly	Gly	
			195				200						205				
	Gly	Ala	Pro	Met	Ala	Asp	Asn	Asn	Glu	Gly	Ala	Asp	Gly	Val	Gly	Ser	
45		210					215					220					
	Ser	Ser	Gly	Asn	Trp	His	Cys	Asp	Ser	Thr	Trp	Leu	Gly	Asp	Arg	Val	
	225					230					235					240	
50	Ile	Thr	Thr	Ser	Thr	Arg	Thr	Trp	Ala	Leu	Pro	Thr	Tyr	Asn	Asn	His	
					245					250					255		

EP 1 310 571 B1

5 Leu Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp  
 260 265 270  
 Asn Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn  
 275 280 285  
 10 Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn  
 290 295 300  
 Asn Asn Trp Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn  
 305 310 315 320  
 15 Ile Gln Val Lys Glu Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala  
 325 330 335  
 Asn Asn Leu Thr Ser Thr Ile Gln Val Phe Thr Asp Ser Glu Tyr Gln  
 340 345 350  
 20 Leu Pro Tyr Val Pro Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe  
 355 360 365  
 25 Pro Ala Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn  
 370 375 380  
 Asn Gly Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr  
 385 390 395 400  
 30 Phe Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr  
 405 410 415  
 35 Thr Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser  
 420 425 430  
 Leu Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu  
 435 440 445  
 40 Ser Arg Thr Gln Ser Thr Gly Gly Thr Gln Gly Thr Gln Gln Leu Leu  
 450 455 460  
 45 Phe Ser Gln Ala Gly Pro Ala Asn Met Ser Ala Gln Ala Lys Asn Trp  
 465 470 475 480  
 50 Leu Pro Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Thr Thr Leu Ser  
 485 490 495  
 Gln Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His  
 500 505 510  
 55 Leu Asn Gly Arg Asp Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr  
 515 520 525

# EP 1 310 571 B1

His Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Met  
 530 535 540  
 5  
 Phe Gly Lys Gln Gly Ala Gly Lys Asp Asn Val Asp Tyr Ser Ser Val  
 545 550 555 560  
 10  
 Met Leu Thr Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr  
 565 570 575  
 Glu Gln Tyr Gly Val Val Ala Asp Asn Leu Gln Gln Thr Asn Gly Ala  
 580 585 590  
 15  
 Pro Ile Val Gly Thr Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val  
 595 600 605  
 20  
 Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile  
 610 615 620  
 Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe  
 625 630 635 640  
 25  
 Gly Leu Lys His Pro Pro Pro Gln Ile Leu Val Lys Asn Thr Pro Val  
 645 650 655  
 30  
 Pro Ala Asp Pro Pro Thr Thr Phe Ser Gln Ala Lys Leu Ala Ser Phe  
 660 665 670  
 Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu  
 675 680 685  
 35  
 Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr  
 690 695 700  
 40  
 Ser Asn Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu  
 705 710 715 720  
 Gly Thr Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg  
 725 730 735  
 45  
 Asn Leu

<210> 93

<211> 738

<212> PRT

<213> capsid protein of AAV serotype, clone 43.12

<400> 93

EP 1 310 571 B1

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
1 5 10 15

5 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
20 25 30

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
35 40 45

10 Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60

15 Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
85 90 95

20 Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
100 105 110

25 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
115 120 125

Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
130 135 140

30 Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile  
145 150 155 160

35 Gly Lys Lys Gly His Gln Pro Ala Arg Lys Arg Leu Asn Phe Gly Gln  
165 170 175

Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro  
180 185 190

40 Pro Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly  
195 200 205

45 Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser  
210 215 220

Ser Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val  
225 230 235 240

50 Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His  
245 250 255

55



EP 1 310 571 B1

Leu Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp  
 260 265 270  
 5  
 Asn Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn  
 275 280 285  
 10  
 Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn  
 290 295 300  
 Asn Asn Trp Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn  
 305 310 315 320  
 15  
 Ile Gln Val Lys Glu Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala  
 325 330 335  
 Asn Asn Leu Thr Ser Thr Ile Gln Val Phe Thr Asp Ser Glu Tyr Gln  
 340 345 350  
 20  
 Leu Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe  
 355 360 365  
 25  
 Pro Ala Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn  
 370 375 380  
 Asn Gly Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr  
 385 390 395 400  
 30  
 Phe Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr  
 405 410 415  
 35  
 Thr Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser  
 420 425 430  
 Leu Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu  
 435 440 445  
 40  
 Ser Arg Thr Gln Ser Thr Gly Gly Thr Gln Gly Thr Gln Gln Leu Leu  
 450 455 460  
 45  
 Phe Ser Gln Ala Gly Pro Ala Asn Met Ser Ala Gln Ala Lys Asn Trp  
 465 470 475 480  
 Leu Pro Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Thr Thr Leu Ser  
 485 490 495  
 50  
 Gln Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His  
 500 505 510  
 55

# EP 1 310 571 B1

Leu Asn Gly Arg Asp Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr  
 515 520 525  
 5  
 His Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Met  
 530 535 540  
 10  
 Phe Gly Lys Gln Gly Ala Gly Lys Asp Asn Val Asp Tyr Ser Ser Val  
 545 550 555 560  
 Met Leu Thr Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr  
 565 570 575  
 15  
 Glu Gln Tyr Gly Val Val Ala Asp Asn Leu Gln Gln Thr Asn Gly Ala  
 580 585 590  
 Pro Ile Val Gly Thr Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val  
 595 600 605  
 20  
 Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile  
 610 615 620  
 25  
 Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe  
 625 630 635 640  
 Gly Leu Lys His Pro Pro Pro Gln Ile Leu Val Lys Asn Thr Pro Val  
 645 650 655  
 30  
 Pro Ala Asp Pro Pro Thr Thr Phe Ser Gln Ala Lys Leu Ala Ser Phe  
 660 665 670  
 35  
 Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu  
 675 680 685  
 Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr  
 690 695 700  
 40  
 Ser Asn Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu  
 705 710 715 720  
 45  
 Gly Thr Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg  
 725 730 735

Asn Leu

<210> 94

<211> 738

<212> PRT

<213> capsid protein of AAV serotype, clone 43.5

<400> 94

EP 1 310 571 B1

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
1 5 10 15

5 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
20 25 30

10 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60

15 Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

20 Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
85 90 95

25 Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
100 105 110

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
115 120 125

30 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
130 135 140

Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile  
145 150 155 160

35 Gly Lys Lys Gly His Gln Pro Ala Arg Lys Arg Leu Asn Phe Gly Gln  
165 170 175

40 Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro  
180 185 190

Pro Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly  
195 200 205

45 Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser  
210 215 220

Ser Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val  
225 230 235 240

50 Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His  
245 250 255

55

EP 1 310 571 B1

Leu Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp  
 260 265 270  
 5  
 Asn Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn  
 275 280 285  
 10  
 Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn  
 290 295 300  
 Asn Asn Trp Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn  
 305 310 315 320  
 15  
 Ile Gln Val Lys Glu Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala  
 325 330 335  
 Asn Asn Leu Thr Ser Thr Ile Gln Val Phe Thr Asp Ser Glu Tyr Gln  
 340 345 350  
 20  
 Leu Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe  
 355 360 365  
 25  
 Pro Ala Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn  
 370 375 380  
 Asn Gly Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr  
 385 390 395 400  
 30  
 Phe Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr  
 405 410 415  
 35  
 Thr Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser  
 420 425 430  
 Leu Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu  
 435 440 445  
 40  
 Ser Arg Thr Gln Ser Thr Gly Gly Thr Gln Gly Thr Gln Gln Leu Leu  
 450 455 460  
 45  
 Phe Ser Gln Ala Gly Pro Ala Asn Met Ser Ala Gln Ala Lys Asn Trp  
 465 470 475 480  
 Leu Pro Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Thr Thr Leu Ser  
 485 490 495  
 50  
 Gln Asn Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His  
 500 505 510  
 55

EP 1 310 571 B1

5 Leu Asn Gly Arg Asp Ser Leu Val Asn Pro Gly Val Ala Met Ala Thr  
 515 520 525  
 His Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Ser Gly Val Leu Met  
 530 535 540  
 10 Phe Gly Lys Gln Gly Ala Gly Lys Asp Asn Val Asp Tyr Ser Ser Val  
 545 550 555 560  
 Met Leu Thr Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr  
 565 570 575  
 15 Glu Gln Tyr Gly Val Val Ala Asp Asn Leu Gln Gln Thr Asn Gly Ala  
 580 585 590  
 Pro Ile Val Gly Thr Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val  
 595 600 605  
 Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile  
 610 615 620  
 25 Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe  
 625 630 635 640  
 Gly Leu Lys His Pro Pro Pro Gln Ile Leu Val Lys Asn Thr Pro Val  
 645 650 655  
 Pro Ala Asp Pro Pro Thr Thr Phe Ser Gln Ala Lys Leu Ala Ser Phe  
 660 665 670  
 35 Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu  
 675 680 685  
 Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr  
 690 695 700  
 Ser Asn Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu  
 705 710 715 720  
 45 Gly Thr Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg  
 725 730 735  
 50 Asn Leu

<210> 95

<211> 738

<212> PRT

<213> capsid protein of AAV serotype, clone AAV8

<400> 95

EP 1 310 571 B1

	Met	Ala	Ala	Asp	Gly	Tyr	Leu	Pro	Asp	Trp	Leu	Glu	Asp	Asn	Leu	Ser
	1				5					10					15	
5	Glu	Gly	Ile	Arg	Glu	Trp	Trp	Ala	Leu	Lys	Pro	Gly	Ala	Pro	Lys	Pro
				20					25					30		
	Lys	Ala	Asn	Gln	Gln	Lys	Gln	Asp	Asp	Gly	Arg	Gly	Leu	Val	Leu	Pro
10			35					40					45			
	Gly	Tyr	Lys	Tyr	Leu	Gly	Pro	Phe	Asn	Gly	Leu	Asp	Lys	Gly	Glu	Pro
	50						55					60				
15	Val	Asn	Ala	Ala	Asp	Ala	Ala	Ala	Leu	Glu	His	Asp	Lys	Ala	Tyr	Asp
	65					70					75					80
	Gln	Gln	Leu	Gln	Ala	Gly	Asp	Asn	Pro	Tyr	Leu	Arg	Tyr	Asn	His	Ala
20					85					90					95	
	Asp	Ala	Glu	Phe	Gln	Glu	Arg	Leu	Gln	Glu	Asp	Thr	Ser	Phe	Gly	Gly
				100					105					110		
25	Asn	Leu	Gly	Arg	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Val	Leu	Glu	Pro
			115					120					125			
	Leu	Gly	Leu	Val	Glu	Glu	Gly	Ala	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Arg
30		130					135					140				
	Pro	Val	Glu	Pro	Ser	Pro	Gln	Arg	Ser	Pro	Asp	Ser	Ser	Thr	Gly	Ile
	145					150					155					160
35	Gly	Lys	Lys	Gly	Gln	Gln	Pro	Ala	Arg	Lys	Arg	Leu	Asn	Phe	Gly	Gln
				165					170						175	
	Thr	Gly	Asp	Ser	Glu	Ser	Val	Pro	Asp	Pro	Gln	Pro	Leu	Gly	Glu	Pro
40				180					185					190		
	Pro	Ala	Ala	Pro	Ser	Gly	Val	Gly	Pro	Asn	Thr	Met	Ala	Ala	Gly	Gly
		195						200					205			
45	Gly	Ala	Pro	Met	Ala	Asp	Asn	Asn	Glu	Gly	Ala	Asp	Gly	Val	Gly	Ser
	210						215					220				
	Ser	Ser	Gly	Asn	Trp	His	Cys	Asp	Ser	Thr	Trp	Leu	Gly	Asp	Arg	Val
50	225				230						235					240

EP 1 310 571 B1

Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His  
 245 250 255  
 5  
 Leu Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ala Thr Asn Asp  
 260 265 270  
 10  
 Asn Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn  
 275 280 285  
 Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn  
 290 295 300  
 15  
 Asn Asn Trp Gly Phe Arg Pro Lys Arg Leu Ser Phe Lys Leu Phe Asn  
 305 310 315 320  
 20  
 Ile Gln Val Lys Glu Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala  
 325 330 335  
 Asn Asn Leu Thr Ser Thr Ile Gln Val Phe Thr Asp Ser Glu Tyr Gln  
 340 345 350  
 25  
 Leu Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe  
 355 360 365  
 30  
 Pro Ala Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn  
 370 375 380  
 Asn Gly Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr  
 385 390 395 400  
 35  
 Phe Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Gln Phe Thr Tyr  
 405 410 415  
 40  
 Thr Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser  
 420 425 430  
 Leu Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu  
 435 440 445  
 45  
 Ser Arg Thr Gln Thr Thr Gly Gly Thr Ala Asn Thr Gln Thr Leu Gly  
 450 455 460  
 50  
 Phe Ser Gln Gly Gly Pro Asn Thr Met Ala Asn Gln Ala Lys Asn Trp  
 465 470 475 480  
 55  
 Leu Pro Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Thr Thr Thr Gly  
 485 490 495

EP 1 310 571 B1

5 Gln Asn Asn Asn Ser Asn Phe Ala Trp Thr Ala Gly Thr Lys Tyr His  
 500 505 510  
 10 Leu Asn Gly Arg Asn Ser Leu Ala Asn Pro Gly Ile Ala Met Ala Thr  
 515 520 525  
 15 His Lys Asp Asp Glu Glu Arg Phe Phe Pro Ser Asn Gly Ile Leu Ile  
 530 535 540  
 20 Phe Gly Lys Gln Asn Ala Ala Arg Asp Asn Ala Asp Tyr Ser Asp Val  
 545 550 555 560  
 25 Met Leu Thr Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr  
 565 570 575  
 30 Glu Glu Tyr Gly Ile Val Ala Asp Asn Leu Gln Gln Gln Asn Thr Ala  
 580 585 590  
 35 Pro Gln Ile Gly Thr Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val  
 595 600 605  
 40 Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile  
 610 615 620  
 45 Pro His Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe  
 625 630 635 640  
 50 Gly Leu Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val  
 645 650 655  
 55 Pro Ala Asp Pro Pro Thr Thr Phe Asn Gln Ser Lys Leu Asn Ser Phe  
 660 665 670  
 60 Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu  
 675 680 685  
 65 Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr  
 690 695 700  
 70 Ser Asn Tyr Tyr Lys Ser Thr Ser Val Asp Phe Ala Val Asn Thr Glu  
 705 710 715 720  
 75 Gly Val Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg  
 725 730 735  
 80 Asn Leu

<210> 96  
 <211> 736



# EP 1 310 571 B1

<212> PRT

<213> capsid protein of AAV serotype, clone 43.21

<400> 96

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Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
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Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
20 25 30

15

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60

20

Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

25

Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
100 105 110

30

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
115 120 125

35

Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
130 135 140

Pro Val Glu Gln Ser Pro Gln Glu Pro Asp Ser Ser Ser Gly Ile Gly  
145 150 155 160

40

Lys Thr Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln Thr  
165 170 175

45

Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro Pro  
180 185 190

Ala Ala Pro Ser Gly Leu Gly Pro Asn Thr Met Ala Ser Gly Gly Gly  
195 200 205

50

Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ser  
210 215 220

55

EP 1 310 571 B1

Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile  
 225 230 235 240  
 5  
 Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu  
 245 250 255  
 10  
 Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp Asn  
 260 265 270  
 Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg  
 275 280 285  
 15  
 Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn  
 290 295 300  
 20  
 Asn Trp Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn Ile  
 305 310 315 320  
 Gln Val Lys Glu Val Thr Thr Asn Glu Gly Thr Lys Thr Ile Ala Asn  
 325 330 335  
 25  
 Asn Leu Thr Ser Thr Val Arg Val Phe Thr Asp Ser Glu Tyr Gln Leu  
 340 345 350  
 30  
 Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro  
 355 360 365  
 Ala Asp Val Phe Met Val Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn  
 370 375 380  
 35  
 Gly Ser Gln Ala Leu Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe  
 385 390 395 400  
 40  
 Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Gln Phe Ser Tyr Thr  
 405 410 415  
 Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu  
 420 425 430  
 45  
 Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Val  
 435 440 445  
 50  
 Arg Thr Gln Thr Thr Gly Thr Gly Gly Thr Gln Thr Leu Ala Phe Ser  
 450 455 460  
 55  
 Gln Ala Gly Pro Ser Ser Met Ala Asn Gln Ala Arg Asn Trp Val Pro  
 465 470 475 480

EP 1 310 571 B1

	Gly	Pro	Cys	Tyr	Arg	Gln	Gln	Arg	Val	Ser	Thr	Thr	Thr	Asn	Gln	Ser	
					485					490					495		
5	Asn	Asn	Ser	Asn	Phe	Ala	Trp	Thr	Gly	Ala	Ala	Lys	Phe	Lys	Leu	Asn	
				500					505					510			
	Gly	Arg	Asp	Ser	Leu	Met	Asn	Pro	Gly	Val	Ala	Met	Ala	Ser	His	Lys	
10			515					520					525				
	Asp	Asp	Asp	Asp	Arg	Phe	Phe	Pro	Ser	Ser	Gly	Val	Leu	Ile	Phe	Gly	
		530					535					540					
15	Lys	Gln	Gly	Ala	Gly	Asn	Asp	Gly	Val	Asp	Tyr	Ser	Gln	Val	Leu	Ile	
	545					550					555					560	
	Thr	Asp	Glu	Glu	Glu	Ile	Lys	Ala	Thr	Asn	Pro	Val	Ala	Thr	Glu	Glu	
20					565					570					575		
	Tyr	Gly	Ala	Val	Ala	Ile	Asn	Asn	Gln	Ala	Ala	Asn	Thr	Gln	Ala	Gln	
				580					585					590			
25	Thr	Gly	Leu	Val	His	Asn	Gln	Gly	Val	Ile	Pro	Gly	Met	Val	Trp	Gln	
			595					600					605				
	Asn	Arg	Asp	Val	Tyr	Leu	Gln	Gly	Pro	Ile	Trp	Ala	Lys	Ile	Pro	His	
30		610					615					620					
	Thr	Asp	Gly	Asn	Phe	His	Pro	Ser	Pro	Leu	Met	Gly	Gly	Phe	Gly	Leu	
	625					630					635					640	
35	Lys	His	Pro	Pro	Pro	Gln	Ile	Leu	Ile	Lys	Asn	Thr	Pro	Val	Pro	Ala	
					645					650					655		
	Asp	Pro	Pro	Leu	Thr	Phe	Asn	Gln	Ala	Lys	Leu	Asn	Ser	Phe	Ile	Thr	
40				660					665					670			
	Gln	Tyr	Ser	Thr	Gly	Gln	Val	Ser	Val	Glu	Ile	Glu	Trp	Glu	Leu	Gln	
			675					680					685				
45	Lys	Glu	Asn	Ser	Lys	Arg	Trp	Asn	Pro	Glu	Ile	Gln	Tyr	Thr	Ser	Asn	
	690						695					700					
	Tyr	Tyr	Lys	Ser	Thr	Asn	Val	Asp	Phe	Ala	Val	Asn	Thr	Glu	Gly	Val	
50	705					710					715					720	
	Tyr	Ser	Glu	Pro	Arg	Pro	Ile	Gly	Thr	Arg	Tyr	Leu	Thr	Arg	Asn	Leu	
					725					730					735		

<210> 97  
<211> 736

# EP 1 310 571 B1

<212> PRT

<213> capsid protein of AAV serotype, clone 43.25

<400> 97

5

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
1 5 10 15

10

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
20 25 30

15

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60

20

Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

25

Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
100 105 110

30

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
115 120 125

Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
130 135 140

35

Pro Val Glu Gln Ser Pro Gln Glu Pro Asp Ser Ser Ser Gly Ile Gly  
145 150 155 160

40

Lys Thr Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln Thr  
165 170 175

Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro Pro  
180 185 190

45

Ala Ala Pro Ser Gly Leu Gly Pro Asn Thr Met Ala Ser Gly Gly Gly  
195 200 205

50

Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ser  
210 215 220

Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile  
225 230 235 240

55

EP 1 310 571 B1

5 Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu  
245 250 255

10 Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp Asn  
260 265 270

15 Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg  
275 280 285

20 Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn  
290 295 300

25 Asn Trp Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn Ile  
305 310 315 320

30 Gln Val Lys Glu Val Thr Thr Asn Glu Gly Thr Lys Thr Ile Ala Asn  
325 330 335

35 Asn Leu Thr Ser Thr Val Gln Val Phe Thr Asp Ser Glu Tyr Gln Leu  
340 345 350

40 Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro  
355 360 365

45 Ala Asp Val Phe Met Val Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn  
370 375 380

50 Gly Ser Gln Ala Leu Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe  
385 390 395 400

55 Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Gln Phe Ser Tyr Thr  
405 410 415

60 Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu  
420 425 430

65 Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Val  
435 440 445

70 Arg Thr Gln Thr Thr Gly Thr Gly Gly Thr Gln Thr Leu Ala Phe Ser  
450 455 460

75 Gln Ala Gly Pro Ser Ser Met Ala Asn Gln Ala Arg Asn Trp Val Pro  
465 470 475 480

80 Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Thr Thr Thr Asn Gln Asn  
485 490 495

EP 1 310 571 B1

5 Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Ala Lys Phe Lys Leu Asn  
 500 505 510  
 Gly Arg Asp Ser Leu Met Asn Pro Gly Val Ala Met Ala Ser His Lys  
 515 520 525  
 10 Asp Asp Asp Asp Arg Phe Phe Pro Ser Ser Gly Val Leu Ile Phe Gly  
 530 535 540  
 Lys Gln Gly Ala Gly Asn Asp Gly Val Asp Tyr Ser Gln Val Leu Ile  
 545 550 555 560  
 15 Thr Asp Glu Glu Glu Ile Lys Ala Thr Asn Pro Val Ala Thr Glu Glu  
 565 570 575  
 20 Tyr Gly Ala Val Ala Ile Asn Asn Gln Ala Ala Asn Thr Gln Ala Gln  
 580 585 590  
 Thr Gly Leu Val His Asn Gln Gly Val Ile Pro Gly Met Val Trp Gln  
 595 600 605  
 25 Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His  
 610 615 620  
 30 Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu  
 625 630 635 640  
 Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala  
 645 650 655  
 35 Asp Pro Pro Leu Thr Phe Asn Gln Ala Lys Leu Asn Ser Phe Ile Thr  
 660 665 670  
 40 Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln  
 675 680 685  
 Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn  
 690 695 700  
 45 Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu Gly Val  
 705 710 715 720  
 50 Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu  
 725 730 735

<210> 98

<211> 736

<212> PRT

<213> capsid protein of AAV serotype, clone 43.23

## EP 1 310 571 B1

&lt;400&gt; 98

5 Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
 1 5 10 15  
 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
 20 25 30  
 10 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
 35 40 45  
 Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
 50 55 60  
 15 Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
 65 70 75 80  
 20 Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
 85 90 95  
 Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
 100 105 110  
 25 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
 115 120 125  
 30 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
 130 135 140  
 Pro Val Glu Gln Ser Pro Gln Glu Pro Asp Ser Ser Ser Gly Ile Gly  
 145 150 155 160  
 35 Lys Thr Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln Thr  
 165 170 175  
 40 Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro Pro  
 180 185 190  
 Ala Ala Pro Ser Gly Leu Gly Pro Asn Thr Met Ala Ser Gly Gly Gly  
 195 200 205  
 45 Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ser  
 210 215 220  
 50 Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile  
 225 230 235 240  
 55

EP 1 310 571 B1

5 Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu  
245 250 255

Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp Asn  
260 265 270

10 Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg  
275 280 285

Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn  
290 295 300

15 Asn Trp Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn Ile  
305 310 315 320

20 Gln Val Lys Glu Val Thr Thr Asn Glu Gly Thr Lys Thr Ile Ala Asn  
325 330 335

Asn Leu Thr Ser Thr Val Gln Val Phe Thr Asp Leu Glu Tyr Gln Leu  
340 345 350

25 Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro  
355 360 365

30 Ala Asp Val Phe Met Val Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn  
370 375 380

Gly Ser Gln Ala Leu Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe  
385 390 395 400

35 Pro Ser Gln Met Pro Arg Thr Gly Asn Asn Phe Gln Phe Ser Tyr Thr  
405 410 415

40 Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu  
420 425 430

Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Val  
435 440 445

45 Arg Thr Gln Thr Thr Gly Thr Gly Gly Thr Gln Thr Leu Ala Phe Ser  
450 455 460

50 Gln Ala Gly Pro Ser Ser Met Ala Asn Gln Ala Arg Asn Trp Val Pro  
465 470 475 480

Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Thr Thr Thr Asn Gln Asn  
485 490 495

55



EP 1 310 571 B1

Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Ala Lys Phe Lys Leu Asn  
 500 505 510  
 5  
 Gly Arg Asp Ser Leu Met Asn Pro Gly Val Ala Met Ala Ser His Lys  
 515 520 525  
 10  
 Asp Asp Asp Asp Arg Phe Phe Pro Ser Ser Gly Val Leu Ile Phe Gly  
 530 535 540  
 Lys Gln Gly Ala Gly Asn Asp Gly Val Asp Tyr Ser Gln Val Leu Ile  
 545 550 555 560  
 15  
 Thr Asp Glu Glu Glu Ile Lys Ala Thr Asn Pro Val Ala Thr Glu Glu  
 565 570 575  
 20  
 Tyr Gly Ala Val Ala Ile Asn Asn Gln Ala Ala Asn Thr Gln Ala Gln  
 580 585 590  
 Thr Gly Leu Val His Asn Gln Gly Val Ile Pro Gly Met Val Trp Gln  
 595 600 605  
 25  
 Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His  
 610 615 620  
 30  
 Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu  
 625 630 635 640  
 Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala  
 645 650 655  
 35  
 Asp Pro Pro Leu Thr Phe Asn Gln Ala Lys Leu Asn Ser Phe Ile Thr  
 660 665 670  
 40  
 Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln  
 675 680 685  
 Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn  
 690 695 700  
 45  
 Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu Gly Val  
 705 710 715 720  
 50  
 Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu  
 725 730 735

<210> 99

<211> 736

<212> PRT

<213> capsid protein of AAV serotype, clone 43.20

## EP 1 310 571 B1

&lt;400&gt; 99

5 Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
 1 5 10 15  
 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
 20 25 30  
 10 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
 35 40 45  
 Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
 50 55 60  
 15 Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
 65 70 75 80  
 20 Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
 85 90 95  
 Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
 100 105 110  
 25 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
 115 120 125  
 30 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
 130 135 140  
 Leu Val Glu Gln Ser Pro Gln Glu Pro Asp Ser Ser Ser Gly Ile Gly  
 145 150 155 160  
 35 Lys Thr Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln Thr  
 165 170 175  
 40 Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro Pro  
 180 185 190  
 Ala Ala Pro Ser Gly Leu Gly Pro Asn Thr Met Ala Ser Gly Gly Gly  
 195 200 205  
 45 Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ser  
 210 215 220  
 50 Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile  
 225 230 235 240  
 55

EP 1 310 571 B1

5 Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu  
245 250 255

10 Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp Asn  
260 265 270

15 Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg  
275 280 285

20 Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn  
290 295 300

25 Asn Trp Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn Ile  
305 310 315 320

30 Gln Val Lys Glu Val Thr Thr Asn Glu Gly Thr Lys Thr Ile Ala Asn  
325 330 335

35 Asn Leu Thr Ser Thr Val Gln Val Phe Thr Asp Ser Glu Tyr Gln Leu  
340 345 350

40 Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro  
355 360 365

45 Ala Asp Val Phe Thr Val Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn  
370 375 380

50 Gly Ser Gln Ala Leu Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe  
385 390 395 400

55 Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Gln Phe Ser Tyr Thr  
405 410 415

Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu  
420 425 430

Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Val  
435 440 445

Arg Thr Gln Thr Thr Gly Thr Gly Gly Thr Gln Thr Leu Ala Phe Ser  
450 455 460

Gln Ala Gly Pro Ser Ser Met Ala Asn Gln Ala Arg Asn Trp Val Pro  
465 470 475 480

Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Thr Thr Thr Asn Gln Asn  
485 490 495

# EP 1 310 571 B1

5 Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Ala Lys Phe Lys Leu Asn  
 500 505 510  
 Gly Arg Asp Ser Leu Met Asn Pro Gly Val Ala Met Ala Ser His Lys  
 515 520 525  
 10 Asp Asp Asp Asp Arg Phe Phe Pro Ser Ser Gly Val Leu Ile Phe Gly  
 530 535 540  
 Lys Gln Gly Ala Gly Asn Asp Gly Val Asp Tyr Ser Gln Val Leu Ile  
 545 550 555 560  
 15 Thr Asp Glu Glu Glu Ile Lys Ala Thr Asn Pro Val Ala Thr Glu Glu  
 565 570 575  
 20 Tyr Gly Ala Val Ala Ile Asn Asn Gln Ala Ala Asn Thr Gln Ala Gln  
 580 585 590  
 Thr Gly Leu Val His Asn Gln Gly Val Ile Pro Gly Met Val Trp Gln  
 595 600 605  
 25 Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His  
 610 615 620  
 30 Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu  
 625 630 635 640  
 Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala  
 645 650 655  
 35 Asp Pro Pro Leu Thr Phe Asn Gln Ala Lys Leu Asn Ser Phe Ile Thr  
 660 665 670  
 40 Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln  
 675 680 685  
 Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn  
 690 695 700  
 45 Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu Gly Val  
 705 710 715 720  
 50 Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu  
 725 730 735

<210> 100

<211> 736

<212> PRT

<213> capsid protein of AAV serotype, clone AAV9

400> 100

EP 1 310 571 B1

	Met	Ala	Ala	Asp	Gly	Tyr	Leu	Pro	Asp	Trp	Leu	Glu	Asp	Asn	Leu	Ser	
	1				5					10					15		
5	Glu	Gly	Ile	Arg	Glu	Trp	Trp	Asp	Leu	Lys	Pro	Gly	Ala	Pro	Lys	Pro	
				20					25					30			
	Lys	Ala	Asn	Gln	Gln	Lys	Gln	Asp	Asp	Gly	Arg	Gly	Leu	Val	Leu	Pro	
10			35					40					45				
	Gly	Tyr	Lys	Tyr	Leu	Gly	Pro	Phe	Asn	Gly	Leu	Asp	Lys	Gly	Glu	Pro	
		50					55					60					
15	Val	Asn	Ala	Ala	Asp	Ala	Ala	Ala	Leu	Glu	His	Asp	Lys	Ala	Tyr	Asp	
	65					70					75					80	
	Gln	Gln	Leu	Lys	Ala	Gly	Asp	Asn	Pro	Tyr	Leu	Arg	Tyr	Asn	His	Ala	
20					85				90						95		
	Asp	Ala	Glu	Phe	Gln	Glu	Arg	Leu	Gln	Glu	Asp	Thr	Ser	Phe	Gly	Gly	
				100					105					110			
25	Asn	Leu	Gly	Arg	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Val	Leu	Glu	Pro	
			115					120					125				
	Leu	Gly	Leu	Val	Glu	Glu	Gly	Ala	Lys	Thr	Ala	Pro	Gly	Lys	Lys	Arg	
30		130					135					140					
	Pro	Val	Glu	Gln	Ser	Pro	Gln	Glu	Pro	Asp	Ser	Ser	Ser	Gly	Ile	Gly	
	145					150					155					160	
35	Lys	Ser	Gly	Gln	Gln	Pro	Ala	Lys	Lys	Arg	Leu	Asn	Phe	Gly	Gln	Thr	
				165						170					175		
	Gly	Asp	Ser	Glu	Ser	Val	Pro	Asp	Pro	Gln	Pro	Leu	Gly	Glu	Pro	Pro	
40				180					185					190			
	Glu	Ala	Pro	Ser	Gly	Leu	Gly	Pro	Asn	Thr	Met	Ala	Ser	Gly	Gly	Gly	
			195					200					205				
45	Ala	Pro	Met	Ala	Asp	Asn	Asn	Glu	Gly	Ala	Asp	Gly	Val	Gly	Asn	Ser	
		210					215					220					
	Ser	Gly	Asn	Trp	His	Cys	Asp	Ser	Thr	Trp	Leu	Gly	Asp	Arg	Val	Ile	
50		225				230					235					240	
	Thr	Thr	Ser	Thr	Arg	Thr	Trp	Ala	Leu	Pro	Thr	Tyr	Asn	Asn	His	Leu	
				245						250					255		

EP 1 310 571 B1

5 Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp Asn  
260 265 270

Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg  
275 280 285

10 Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn  
290 295 300

15 Asn Trp Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn Ile  
305 310 315 320

Gln Val Lys Glu Val Thr Thr Asn Glu Gly Thr Lys Thr Ile Ala Asn  
325 330 335

20 Asn Leu Thr Ser Thr Val Gln Val Phe Thr Asp Ser Glu Tyr Gln Leu  
340 345 350

25 Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro  
355 360 365

Ala Asp Val Phe Met Val Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn  
370 375 380

30 Gly Ser Gln Ala Leu Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe  
385 390 395 400

35 Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Gln Phe Ser Tyr Thr  
405 410 415

Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu  
420 425 430

40 Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Val  
435 440 445

45 Arg Thr Gln Thr Thr Gly Thr Gly Gly Thr Gln Thr Leu Ala Phe Ser  
450 455 460

Gln Ala Gly Pro Ser Ser Met Ala Asn Gln Ala Arg Asn Trp Val Pro  
465 470 475 480

50 Gly Pro Cys Tyr Arg Gln Gln Arg Val Ser Thr Thr Thr Asn Gln Asn  
485 490 495

55 Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Ala Lys Phe Lys Leu Asn  
500 505 510

# EP 1 310 571 B1

Gly Arg Asp Ser Leu Met Asn Pro Gly Val Ala Met Ala Ser His Lys  
 515 520 525  
 5  
 Asp Asp Glu Asp Arg Phe Phe Pro Ser Ser Gly Val Leu Ile Phe Gly  
 530 535 540  
 10  
 Lys Gln Gly Ala Gly Asn Asp Gly Val Asp Tyr Ser Gln Val Leu Ile  
 545 550 555 560  
 Thr Asp Glu Glu Glu Ile Lys Ala Thr Asn Pro Val Ala Thr Glu Glu  
 565 570 575  
 15  
 Tyr Gly Ala Val Ala Ile Asn Asn Gln Ala Ala Asn Thr Gln Ala Gln  
 580 585 590  
 20  
 Thr Gly Leu Val His Asn Gln Gly Val Ile Pro Gly Met Val Trp Gln  
 595 600 605  
 Asn Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His  
 610 615 620  
 25  
 Thr Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu  
 625 630 635 640  
 30  
 Lys His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala  
 645 650 655  
 Asp Pro Pro Leu Thr Phe Asn Gln Ala Lys Leu Asn Ser Phe Ile Thr  
 660 665 670  
 35  
 Gln Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln  
 675 680 685  
 40  
 Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn  
 690 695 700  
 Tyr Tyr Lys Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu Gly Val  
 705 710 715 720  
 45  
 Tyr Ser Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu  
 725 730 735

<210> 101

<211> 728

<212> PRT

<213> capsid protein of AAV serotype, clone 24.1

<400> 101

EP 1 310 571 B1

Met	Ala	Ala	Asp	Gly	Tyr	Leu	Pro	Asp	Trp	Leu	Glu	Asp	Asn	Leu	Ser
1				5					10					15	

5

10

15

20

25

30

35

40

45

50

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EP 1 310 571 B1

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 15  
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 25  
 30  
 35  
 40  
 45  
 50  
 55

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
 20 25 30

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
 35 40 45

Gly Tyr Lys Tyr Leu Arg Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
 50 55 60

Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
 65 70 75 80

Lys Gln Leu Glu Gln Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala  
 85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
 100 105 110

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
 115 120 125

Leu Gly Leu Val Glu Glu Val Ala Lys Thr Ala Pro Gly Lys Lys Arg  
 130 135 140

Pro Ile Glu Ser Pro Asp Ser Ser Thr Gly Ile Gly Lys Lys Gly Gln  
 145 150 155 160

Gln Pro Ala Lys Lys Lys Leu Asn Phe Gly Gln Thr Gly Asp Ser Glu  
 165 170 175

Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro Pro Ala Ala Pro Ser  
 180 185 190

Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly Gly Ala Pro Met Ala  
 195 200 205

Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala Ser Gly Asn Trp  
 210 215 220

His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile Thr Thr Ser Thr  
 225 230 235 240

Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu Tyr Lys Gln Ile  
 245 250 255

Ser Ser Gln Ser Gly Ala Thr Asn Asp Asn His Phe Phe Ser Tyr Ser  
 260 265 270

EP 1 310 571 B1

5

Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His Cys His Phe Ser  
275 280 285

10

Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp Gly Phe Arg Pro  
290 295 300

Arg Lys Leu Arg Phe Lys Leu Phe Asn Ile Gln Val Lys Glu Val Thr  
305 310 315 320

15

Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn Leu Thr Ser Thr Ile  
325 330 335

Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro Tyr Val Leu Gly Ser  
340 345 350

20

Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp Val Phe Met Ile  
355 360 365

Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser Gln Ser Val Gly  
370 375 380

25

Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met Leu Arg  
385 390 395 400

30

Thr Gly Asn Asn Phe Glu Phe Ser Tyr Thr Phe Glu Glu Val Pro Phe  
405 410 415

His Ser Ser Tyr Val His Ser Gln Ser Leu Asp Arg Leu Met Asn Pro  
420 425 430

35

Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala Arg Thr Gln Ser Thr Thr  
435 440 445

40

Gly Ser Thr Arg Glu Leu Gln Phe His Gln Ala Gly Pro Asn Thr Met  
450 455 460

Ala Glu Gln Ser Lys Asn Trp Leu Pro Gly Pro Cys Tyr Arg Gln Gln  
465 470 475 480

45

Arg Leu Ser Lys Asn Ile Asp Ser Asn Asn Asn Ser Asn Phe Ala Trp  
485 490 495

50

Thr Gly Ala Thr Lys Tyr His Leu Asn Gly Arg Asn Ser Leu Thr Asn  
500 505 510

Pro Gly Val Ala Met Ala Thr Asn Lys Asp Asp Glu Asp Gln Phe Phe  
515 520 525

55

# EP 1 310 571 B1

	Pro	Ile	Asn	Gly	Val	Leu	Val	Phe	Gly	Lys	Thr	Gly	Ala	Ala	Asn	Lys
	530						535					540				
5	Thr	Thr	Leu	Glu	Asn	Val	Leu	Met	Thr	Ser	Glu	Glu	Glu	Ile	Lys	Thr
	545					550					555					560
	Thr	Asn	Pro	Val	Ala	Thr	Glu	Glu	Tyr	Gly	Val	Val	Ser	Ser	Asn	Leu
10					565					570					575	
	Gln	Ser	Ser	Thr	Ala	Gly	Pro	Gln	Thr	Gln	Thr	Val	Asn	Ser	Gln	Gly
				580					585					590		
15	Ala	Leu	Pro	Gly	Met	Val	Trp	Gln	Asn	Arg	Asp	Val	Cys	Leu	Gln	Gly
			595					600					605			
	Pro	Ile	Trp	Ala	Lys	Ile	Pro	His	Thr	Asp	Gly	Asn	Phe	His	Pro	Ser
20							615					620				
	Pro	Leu	Met	Gly	Gly	Phe	Gly	Leu	Lys	His	Pro	Pro	Pro	Gln	Ile	Leu
	625					630					635					640
25	Ile	Lys	Asn	Thr	Pro	Val	Pro	Ala	Asn	Pro	Pro	Glu	Val	Phe	Thr	Pro
					645					650					655	
	Ala	Lys	Phe	Ala	Ser	Phe	Ile	Thr	Gln	Tyr	Ser	Thr	Gly	Gln	Val	Ser
30				660					665					670		
	Val	Glu	Ile	Glu	Trp	Glu	Leu	Gln	Lys	Glu	Asn	Ser	Lys	Arg	Trp	Asn
			675					680					685			
35	Pro	Glu	Ile	Gln	Tyr	Thr	Ser	Asn	Tyr	Ala	Lys	Ser	Asn	Asn	Val	Glu
	690						695					700				
	Phe	Ala	Val	Asn	Asn	Glu	Gly	Val	Tyr	Thr	Glu	Pro	Arg	Pro	Ile	Gly
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	Thr	Arg	Tyr	Leu	Thr	Arg	Asn	Leu								
								725								
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	Met	Ala	Ala	Asp	Gly	Tyr	Leu	Pro	Asp	Trp	Leu	Glu	Asp	Asn	Leu	Ser
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Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
 20 25 30  
 5  
 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
 35 40 45  
 10  
 Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
 50 55 60  
 Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
 65 70 75 80  
 15  
 Lys Gln Leu Glu Gln Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala  
 85 90 95  
 Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
 100 105 110  
 20  
 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
 115 120 125  
 25  
 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
 130 135 140  
 30  
 Pro Ile Glu Ser Pro Asp Ser Ser Thr Gly Ile Gly Lys Lys Gly Gln  
 145 150 155 160  
 Gln Pro Ala Lys Lys Lys Leu Asn Phe Gly Gln Thr Gly Asp Ser Glu  
 165 170 175  
 35  
 Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro Pro Ala Ala Pro Ser  
 180 185 190  
 40  
 Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly Gly Ala Pro Met Ala  
 195 200 205  
 Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala Ser Gly Asn Trp  
 210 215 220  
 45  
 His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile Thr Thr Ser Thr  
 225 230 235 240  
 50  
 Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu Tyr Lys Gln Ile  
 245 250 255  
 Ser Ser Gln Ser Gly Ala Thr Asn Asp Asn His Phe Phe Gly Tyr Ser  
 260 265 270  
 55

EP 1 310 571 B1

5  
 Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His Cys His Phe Ser  
 275 280 285

10  
 Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp Gly Phe Arg Pro  
 290 295 300

15  
 Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn Leu Thr Ser Thr Ile  
 305 310 315 320 325 330 335

20  
 Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro Tyr Val Leu Gly Ser  
 340 345 350

25  
 Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp Val Phe Met Ile  
 355 360 365

30  
 Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser Gln Ser Val Gly  
 370 375 380

35  
 Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met Leu Arg  
 385 390 395 400

40  
 Thr Gly Asn Asn Phe Glu Phe Ser Tyr Thr Phe Glu Glu Val Pro Phe  
 405 410 415

45  
 His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg Leu Met Asn Pro  
 420 425 430

50  
 Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala Arg Thr Gln Ser Thr Thr  
 435 440 445

55  
 Gly Ser Thr Arg Glu Leu Gln Phe His Gln Ala Gly Pro Asn Thr Met  
 450 455 460

Ala Glu Gln Ser Lys Asn Trp Leu Pro Gly Pro Cys Tyr Arg Gln Gln  
 465 470 475 480

Arg Leu Ser Lys Asn Ile Asp Ser Asn Asn Asn Ser Asn Phe Ala Trp  
 485 490 495

Thr Gly Ala Thr Lys Tyr His Leu Asn Gly Arg Asn Ser Leu Thr Asn  
 500 505 510

Pro Gly Val Ala Met Ala Thr Asn Lys Asp Asp Glu Asp Gln Phe Phe  
 515 520 525

# EP 1 310 571 B1

5 Pro Ile Asn Gly Val Leu Val Phe Gly Glu Thr Gly Ala Ala Asn Lys  
 530 535 540  
 Thr Thr Leu Glu Asn Val Leu Met Thr Ser Glu Glu Glu Ile Lys Thr  
 545 550 555  
 10 Thr Asn Pro Val Ala Thr Glu Glu Tyr Gly Val Val Ser Ser Asn Leu  
 565 570 575  
 Gln Ser Ser Thr Ala Gly Pro Gln Thr Gln Thr Val Asn Ser Gln Gly  
 580 585 590  
 15 Ala Leu Pro Gly Met Val Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly  
 595 600 605  
 20 Pro Ile Trp Ala Lys Ile Pro His Thr Asp Gly Asn Phe His Pro Ser  
 610 615 620  
 Pro Leu Met Gly Gly Phe Gly Leu Lys His Pro Pro Pro Gln Ile Leu  
 625 630 635  
 25 Ile Lys Asn Thr Pro Val Pro Ala Asn Pro Pro Glu Val Phe Thr Pro  
 645 650 655  
 30 Ala Lys Phe Ala Ser Phe Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser  
 660 665 670  
 Val Glu Ile Glu Trp Glu Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn  
 675 680 685  
 35 Pro Glu Ile Gln Tyr Thr Ser Asn Tyr Ala Lys Ser Asn Asn Val Glu  
 690 695 700  
 40 Phe Ala Val Asn Asn Glu Gly Val Tyr Thr Glu Pro Arg Pro Ile Gly  
 705 710 715 720  
 Thr Arg Tyr Leu Thr Arg Asn Leu  
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 <212> PRT  
 50 <213> capsid protein of AAV serotype, clone 7.2VP1  
 <400> 103

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EP 1 310 571 B1

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Gly Asn Leu Ser  
1 5 10 15

5 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
20 25 30

10

15

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EP 1 310 571 B1

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
 35 40 45  
 5  
 Gly Tyr Arg Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
 50 55 60  
 10  
 Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
 65 70 75 80  
 Lys Gln Leu Glu Gln Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala  
 85 90 95  
 15  
 Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
 100 105 110  
 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
 115 120 125  
 20  
 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
 130 135 140  
 25  
 Pro Ile Glu Ser Pro Asp Ser Ser Thr Gly Ile Gly Lys Asn Gly Gln  
 145 150 155 160  
 Pro Pro Ala Lys Lys Lys Leu Asn Phe Gly Gln Thr Gly Asp Ser Glu  
 165 170 175  
 30  
 Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro Pro Ala Ala Pro Ser  
 180 185 190  
 35  
 Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly Gly Ala Pro Met Ala  
 195 200 205  
 Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala Ser Gly Asn Trp  
 210 215 220  
 40  
 His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile Thr Thr Ser Thr  
 225 230 235 240  
 45  
 Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu Tyr Lys Gln Ile  
 245 250 255  
 Ser Ser Gln Ser Gly Ala Thr Asn Asp Asn His Phe Phe Gly Tyr Ser  
 260 265 270  
 50  
 Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His Cys His Phe Ser  
 275 280 285  
 55



EP 1 310 571 B1

Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp Gly Phe Arg Pro  
290 295 300

5

Arg Lys Leu Arg Phe Lys Leu Phe Asn Ile Gln Val Lys Glu Val Thr  
305 310 315 320

10

Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn Leu Thr Ser Thr Ile  
325 330 335

Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro Tyr Val Leu Gly Ser  
340 345 350

15

Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp Val Phe Met Ile  
355 360 365

20

Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser Gln Ser Val Gly  
370 375 380

25

Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met Leu Arg  
385 390 395 400

Thr Gly Asp Asn Phe Glu Phe Ser Tyr Thr Phe Glu Glu Val Pro Phe  
405 410 415

30

His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg Leu Met Asn Pro  
420 425 430

35

Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala Arg Thr Gln Ser Thr Thr  
435 440 445

Gly Ser Thr Arg Glu Leu Gln Phe His Gln Ala Gly Pro Asn Thr Met  
450 455 460

40

Ala Glu Gln Ser Lys Asn Trp Leu Pro Gly Pro Cys Tyr Arg Gln Gln  
465 470 475 480

45

Arg Leu Ser Lys Asn Ile Asp Ser Asn Asn Asn Ser Asn Phe Ala Trp  
485 490 495

Thr Gly Ala Thr Lys Tyr His Leu Asn Gly Arg Asn Ser Leu Thr Asn  
500 505 510

50

Pro Gly Val Ala Met Ala Thr Asn Lys Asp Asp Glu Asp Gln Phe Phe  
515 520 525

55

Pro Ile Asn Gly Val Leu Val Phe Gly Lys Thr Gly Ala Ala Asn Lys  
530 535 540

# EP 1 310 571 B1

5 Thr Thr Leu Glu Asn Val Leu Met Thr Ser Glu Glu Glu Ile Lys Thr  
 545 550 555 560  
 Thr Asn Pro Val Ala Thr Glu Glu Tyr Gly Val Val Ser Ser Asn Leu  
 565 570 575  
 10 Gln Ser Ser Thr Ala Gly Pro Gln Thr Gln Thr Val Asn Ser Gln Gly  
 580 585 590  
 Ala Leu Pro Gly Met Val Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly  
 595 600 605  
 15 Pro Ile Trp Ala Lys Ile Pro His Thr Asp Gly Asn Phe His Pro Ser  
 610 615 620  
 20 Pro Leu Met Gly Gly Phe Gly Leu Lys His Pro Pro Pro Gln Ile Leu  
 625 630 635 640  
 Ile Lys Asn Thr Pro Val Pro Ala Asn Pro Pro Glu Val Phe Thr Pro  
 645 650 655  
 25 Ala Lys Phe Ala Ser Phe Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser  
 660 665 670  
 30 Val Glu Ile Glu Trp Glu Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn  
 675 680 685  
 Pro Glu Ile Gln Tyr Thr Ser Asn Tyr Ala Lys Ser Asn Asn Val Glu  
 690 695 700  
 35 Phe Ala Val Asn Asn Glu Gly Val Tyr Thr Glu Pro Arg Pro Ile Gly  
 705 710 715 720  
 40 Thr Arg Tyr Leu Thr Arg Asn Leu  
 725

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 <212> PRT  
 <213> capsid protein of AAV serotype, clone 27.3VP1

<400> 104

50 Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
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 55 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
 20 25 30

EP 1 310 571 B1

5

Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
35 40 45

10

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60

Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

15

Lys Gln Leu Glu Gln Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala  
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
100 105 110

20

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
115 120 125

Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Ser Gly Lys Lys Arg  
130 135 140

25

Pro Ile Glu Ser Pro Asp Ser Ser Thr Gly Ile Gly Lys Lys Gly Gln  
145 150 155 160

30

Gln Pro Ala Lys Lys Lys Leu Asn Phe Gly Gln Thr Gly Asp Ser Glu  
165 170 175

Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro Pro Ala Ala Pro Ser  
180 185 190

35

Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly Gly Ala Pro Met Ala  
195 200 205

40

Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala Ser Gly Asn Trp  
210 215 220

His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile Thr Thr Ser Thr  
225 230 235 240

45

Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu Tyr Lys Gln Ile  
245 250 255

50

Ser Ser Gln Ser Gly Ala Thr Asn Asp Asn His Phe Phe Gly Tyr Ser  
260 265 270

Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His Cys His Phe Ser  
275 280 285

55

EP 1 310 571 B1

5 Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp Gly Phe Arg Pro  
 290 295 300  
 Arg Lys Leu Arg Phe Lys Leu Phe Asn Ile Gln Val Lys Glu Val Thr  
 305 310 315 320  
 10 Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn Leu Thr Ser Thr Ile  
 325 330 335  
 Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro Tyr Val Leu Gly Ser  
 340 345 350  
 15 Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp Val Phe Met Ile  
 355 360 365  
 20 Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser Gln Ser Val Gly  
 370 375 380  
 Arg Ser Ser Phe Cys Cys Leu Glu Tyr Phe Pro Ser Gln Met Leu Arg  
 385 390 395 400  
 25 Thr Gly Asn Asn Phe Glu Phe Ser Tyr Thr Phe Glu Glu Val Pro Phe  
 405 410 415  
 30 His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg Leu Met Asn Pro  
 420 425 430  
 Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala Arg Thr Gln Ser Thr Thr  
 435 440 445  
 35 Gly Ser Thr Arg Glu Leu Gln Phe His Gln Ala Gly Pro Asn Thr Val  
 450 455 460  
 40 Ala Glu Gln Ser Lys Asn Trp Leu Pro Gly Pro Cys Tyr Arg Gln Gln  
 465 470 475 480  
 Arg Leu Ser Lys Asn Ile Asp Ser Asn Asn Asn Ser Asn Phe Ala Trp  
 485 490 495  
 45 Thr Gly Ala Thr Lys Tyr His Leu Asn Gly Arg Asn Ser Leu Thr Asn  
 500 505 510  
 50 Pro Gly Val Ala Met Ala Thr Asn Lys Asp Asp Glu Asp Gln Phe Leu  
 515 520 525  
 55 Pro Ile Asn Gly Val Leu Val Phe Gly Lys Thr Gly Ala Ala Asn Lys  
 530 535 540

# EP 1 310 571 B1

Thr Thr Leu Glu Asn Val Leu Met Thr Ser Glu Glu Glu Ile Lys Thr  
545 550 555 560

Thr Asn Pro Val Ala Thr Glu Glu Tyr Gly Val Val Ser Ser Asn Leu  
565 570 575

Gln Ser Ser Thr Ala Gly Pro Arg Thr Gln Thr Val Asn Ser Gln Gly  
580 585 590

Ala Leu Pro Gly Met Val Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly  
595 600 605

Pro Ile Trp Ala Glu Ile Pro His Thr Asp Gly Asn Phe His Pro Ser  
610 615 620

Pro Leu Met Gly Gly Phe Gly Leu Lys His Pro Pro Pro Gln Ile Leu  
625 630 635 640

Ile Lys Asn Thr Pro Val Pro Ala Asn Pro Pro Glu Val Phe Thr Pro  
645 650 655

Ala Lys Phe Ala Ser Phe Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser  
660 665 670

Val Glu Ile Glu Trp Glu Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn  
675 680 685

Pro Glu Ile Gln Tyr Thr Ser Asn Tyr Ala Lys Ser Asn Asn Val Glu  
690 695 700

Phe Ala Val Asn Asn Glu Gly Val Tyr Thr Glu Pro Arg Pro Ile Gly  
705 710 715 720

Thr Arg Tyr Leu Thr Arg Asn Leu  
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<210> 105

<211> 728

<212> PRT

<213> capsid protein of AAV serotype, clone 16.3VP1

<400> 105

# EP 1 310 571 B1

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
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5 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
 20 25 30

10 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
 35 40 45

15

20

25

30

35

40

45

50

55

EP 1 310 571 B1

5  
 Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
 50 55 60

10  
 Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
 65 70 75 80

15  
 Lys Gln Leu Glu Gln Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala  
 85 90 95

20  
 Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
 100 105 110

25  
 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
 115 120 125

30  
 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
 130 135 140

35  
 Pro Ile Glu Ser Pro Asp Ser Ser Thr Gly Ile Gly Lys Lys Gly Gln  
 145 150 155 160

40  
 Gln Pro Ala Lys Lys Lys Leu Asn Phe Gly Gln Thr Gly Asp Ser Glu  
 165 170 175

45  
 Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro Pro Ala Ala Pro Ser  
 180 185 190

50  
 Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly Gly Ala Pro Met Ala  
 195 200 205

55  
 Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala Ser Gly Asn Trp  
 210 215 220

60  
 His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile Thr Thr Ser Thr  
 225 230 235 240

65  
 Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu Tyr Lys Gln Ile  
 245 250 255

70  
 Ser Ser Gln Ser Gly Ala Thr Asn Asp Asn His Phe Phe Gly Tyr Ser  
 260 265 270

75  
 Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His Cys His Phe Ser  
 275 280 285

80  
 Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp Gly Phe Arg Pro  
 290 295 300

EP 1 310 571 B1

Arg Lys Leu Arg Phe Lys Leu Phe Asn Ile Gln Val Lys Glu Val Thr  
 305 310 315 320  
 5  
 Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn Leu Thr Ser Thr Ile  
 325 330 335  
 10  
 Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro Tyr Val Leu Gly Ser  
 340 345 350  
 Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp Val Phe Met Ile  
 355 360 365  
 15  
 Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser Gln Ser Met Gly  
 370 375 380  
 20  
 Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met Leu Arg  
 385 390 395 400  
 Thr Gly Asn Asn Phe Glu Phe Ser Tyr Thr Phe Glu Glu Val Pro Phe  
 405 410 415  
 25  
 His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg Leu Met Asn Pro  
 420 425 430  
 30  
 Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala Arg Thr Gln Ser Thr Thr  
 435 440 445  
 Gly Ser Thr Arg Glu Leu Gln Phe His Gln Ala Gly Pro Asn Thr Met  
 450 455 460  
 35  
 Ala Glu Gln Ser Lys Asn Trp Leu Pro Gly Pro Cys Tyr Arg Gln Gln  
 465 470 475 480  
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 Arg Leu Ser Lys Asn Ile Asp Ser Asn Asn Asn Ser Asn Phe Ala Trp  
 485 490 495  
 Thr Gly Ala Thr Lys Tyr His Leu Asn Gly Arg Asn Ser Leu Thr Asn  
 500 505 510  
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 Pro Gly Val Ala Met Ala Thr Asn Lys Asp Asp Glu Gly Gln Phe Phe  
 515 520 525  
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 Pro Ile Asn Gly Val Leu Val Phe Gly Lys Thr Gly Ala Ala Asn Lys  
 530 535 540  
 Thr Thr Leu Glu Asn Val Leu Met Thr Ser Glu Glu Glu Ile Lys Thr  
 545 550 555 560  
 55



EP 1 310 571 B1

Thr Asn Pro Val Ala Thr Glu Glu Tyr Gly Val Val Ser Ser Asn Leu  
 565 570 575  
 5  
 Gln Ser Ser Thr Ala Gly Pro Gln Thr Gln Thr Val Asn Ser Gln Gly  
 580 585 590  
 10  
 Ala Leu Pro Gly Met Val Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly  
 595 600 605  
 Pro Ile Trp Ala Lys Ile Pro His Thr Asp Gly Asn Phe His Pro Ser  
 610 615 620  
 15  
 Pro Leu Met Gly Gly Phe Gly Leu Lys His Pro Pro Pro Gln Ile Leu  
 625 630 635 640  
 20  
 Ile Lys Asn Thr Pro Val Pro Ala Asn Pro Pro Gly Val Phe Thr Pro  
 645 650 655  
 Ala Leu Phe Ala Ser Phe Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser  
 660 665 670  
 25  
 Val Glu Ile Glu Trp Glu Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn  
 675 680 685  
 30  
 Pro Glu Ile Gln Tyr Thr Ser Asn Tyr Ala Lys Ser Asn Asn Val Glu  
 690 695 700  
 Phe Ala Val Asn Asn Glu Gly Val Tyr Thr Glu Pro Arg Pro Ile Gly  
 705 710 715 720  
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 Thr Arg Tyr Leu Thr Arg Asn Leu  
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 <210> 106  
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 <400> 106  
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 Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
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 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
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 55  
 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
 35 40 45

EP 1 310 571 B1

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
 50 55 60  
 5  
 Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
 65 70 75 80  
 10  
 Lys Gln Leu Glu Gln Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala  
 85 90 95  
 Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
 100 105 110  
 15  
 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
 115 120 125  
 20  
 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
 130 135 140  
 Pro Ile Glu Ser Pro Asp Ser Ser Thr Gly Ile Gly Arg Lys Gly Gln  
 145 150 155 160  
 25  
 Gln Pro Ala Lys Lys Lys Leu Asn Phe Gly Gln Thr Gly Asp Ser Glu  
 165 170 175  
 30  
 Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro Pro Ala Gly Pro Ser  
 180 185 190  
 Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly Gly Ala Pro Met Ala  
 195 200 205  
 35  
 Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala Ser Gly Asn Trp  
 210 215 220  
 40  
 His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile Thr Thr Ser Thr  
 225 230 235 240  
 Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu Tyr Lys Gln Ile  
 245 250 255  
 45  
 Ser Ser Gln Ser Gly Ala Thr Asn Asp Asn His Phe Phe Gly Tyr Ser  
 260 265 270  
 50  
 Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His Cys His Phe Ser  
 275 280 285  
 Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp Gly Phe Arg Pro  
 290 295 300

55

EP 1 310 571 B1

5 Arg Lys Leu Arg Phe Lys Leu Phe Asn Ile Gln Val Lys Glu Val Thr  
305 310 315 320

Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn Leu Thr Ser Thr Ile  
325 330 335

10 Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro Tyr Val Leu Gly Ser  
340 345 350

15 Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp Val Phe Met Ile  
355 360 365

Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser Gln Ser Val Gly  
370 375 380

20 Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met Leu Arg  
385 390 395 400

25 Thr Gly Asn Asn Phe Glu Phe Ser Tyr Thr Phe Glu Glu Val Pro Phe  
405 410 415

His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg Leu Met Asn Pro  
420 425 430

30 Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala Arg Thr Gln Ser Thr Thr  
435 440 445

35 Gly Ser Thr Arg Glu Leu Gln Phe His Gln Ala Gly Pro Asn Thr Met  
450 455 460

Ala Glu Gln Ser Lys Asn Trp Leu Pro Gly Pro Cys Tyr Arg Gln Gln  
465 470 475 480

40 Arg Leu Ser Lys Asn Ile Asp Ser Asn Asn Asn Ser Asn Phe Ala Trp  
485 490 495

45 Thr Gly Ala Thr Lys Tyr His Leu Asn Gly Arg Asn Ser Leu Thr Asn  
500 505 510

Pro Gly Val Ala Met Ala Thr Asn Lys Asp Asp Glu Asp Gln Phe Phe  
515 520 525

50 Pro Ile Asn Gly Val Leu Val Phe Gly Lys Thr Gly Ala Ala Asn Lys  
530 535 540

55 Thr Thr Leu Glu Asn Val Leu Met Thr Ser Glu Glu Glu Ile Lys Thr  
545 550 555 560

# EP 1 310 571 B1

Thr Asn Pro Val Ala Thr Glu Glu Tyr Gly Val Val Ser Ser Asn Leu  
 565 570 575  
 5  
 Gln Ser Ser Thr Ala Gly Pro Gln Thr Gln Thr Val Asn Ser Gln Gly  
 580 585 590  
 10  
 Ala Leu Pro Gly Met Val Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly  
 595 600 605  
 Pro Ile Trp Ala Lys Ile Pro His Thr Asp Gly Asn Phe His Pro Ser  
 610 615 620  
 15  
 Pro Leu Met Gly Gly Phe Gly Leu Lys His Pro Pro Pro Gln Ile Leu  
 625 630 635 640  
 20  
 Ile Lys Asn Thr Pro Val Pro Ala Asn Pro Pro Glu Val Phe Thr Pro  
 645 650 655  
 Ala Lys Phe Ala Ser Phe Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser  
 660 665 670  
 25  
 Val Glu Ile Glu Trp Glu Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn  
 675 680 685  
 30  
 Pro Glu Ile Gln Tyr Thr Ser Asn Tyr Ala Lys Ser Asn Asn Val Glu  
 690 695 700  
 Phe Ala Val Asn Asn Glu Gly Val Tyr Thr Glu Pro Arg Pro Ile Gly  
 705 710 715 720  
 35  
 Thr Arg Tyr Leu Thr Arg Asn Leu  
 725

40 <210> 107  
 <211> 728  
 <212> PRT  
 <213> capsid protein of AAV serotype, clone 42.3B  
 45 <400> 107

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EP 1 310 571 B1

	Met	Ala	Ala	Asp	Gly	Tyr	Leu	Pro	Asp	Trp	Leu	Glu	Asp	Asn	Leu	Ser
	1				5					10					15	
5	Glu	Gly	Ile	Arg	Glu	Trp	Trp	Asp	Leu	Lys	Pro	Gly	Ala	Pro	Lys	Pro
				20					25					30		
	Lys	Ala	Asn	Gln	Gln	Lys	Gln	Asp	Asp	Gly	Arg	Gly	Leu	Val	Leu	Pro
10			35					40					45			
	Gly	Tyr	Lys	Tyr	Leu	Gly	Pro	Phe	Asn	Gly	Leu	Asp	Lys	Gly	Glu	Pro
	50						55					60				
15																
20																
25																
30																
35																
40																
45																
50																
55																

EP 1 310 571 B1

Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

5  
Lys Gln Leu Glu Gln Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala  
85 90 95

10  
Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
100 105 110

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
115 120 125

15  
Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
130 135 140

20  
Pro Ile Glu Ser Pro Asp Ser Ser Thr Gly Ile Gly Lys Lys Gly Gln  
145 150 155 160

Gln Pro Ala Lys Lys Lys Leu Asn Phe Gly Gln Thr Gly Asp Ser Glu  
165 170 175

25  
Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro Pro Ala Gly Pro Ser  
180 185 190

30  
Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly Gly Ala Pro Met Ala  
195 200 205

Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala Ser Gly Asn Trp  
210 215 220

35  
His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile Thr Thr Ser Thr  
225 230 235 240

40  
Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu Tyr Lys Gln Ile  
245 250 255

Ser Ser Gln Ser Gly Ala Thr Asn Asp Asn His Phe Phe Gly Tyr Ser  
260 265 270

45  
Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His Cys His Phe Ser  
275 280 285

50  
Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp Gly Phe Arg Pro  
290 295 300

Arg Lys Leu Arg Phe Lys Leu Phe Asn Ile Gln Val Lys Glu Val Thr  
305 310 315 320

55

EP 1 310 571 B1

Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn Leu Thr Ser Thr Ile  
 325 330 335  
 5  
 Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro Tyr Val Leu Gly Ser  
 340 345 350  
 10  
 Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp Val Phe Met Ile  
 355 360 365  
 Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser Gln Ser Val Gly  
 370 375 380  
 15  
 Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met Leu Arg  
 385 390 395 400  
 20  
 Thr Gly Asn Asn Phe Glu Phe Ser Tyr Thr Phe Glu Glu Val Pro Phe  
 405 410 415  
 His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg Leu Met Asn Pro  
 420 425 430  
 25  
 Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala Arg Thr Gln Ser Thr Thr  
 435 440 445  
 Gly Ser Thr Arg Glu Leu Gln Phe His Gln Ala Gly Pro Asn Thr Met  
 450 455 460  
 30  
 Ala Glu Gln Ser Lys Asn Trp Leu Pro Gly Pro Cys Tyr Arg Gln Gln  
 465 470 475 480  
 35  
 Arg Leu Ser Lys Asn Ile Asp Ser Asn Asn Thr Ser Asn Phe Ala Trp  
 485 490 495  
 40  
 Thr Gly Ala Thr Lys Tyr His Leu Asn Gly Arg Asn Ser Leu Thr Asn  
 500 505 510  
 Pro Gly Val Ala Met Ala Thr Asn Lys Asp Asp Glu Asp Gln Phe Phe  
 515 520 525  
 45  
 Pro Ile Asn Gly Val Leu Val Phe Gly Lys Thr Gly Ala Ala Asn Lys  
 530 535 540  
 50  
 Thr Thr Leu Glu Asn Val Leu Met Thr Ser Glu Glu Glu Ile Lys Thr  
 545 550 555 560  
 55  
 Thr Asn Pro Val Ala Thr Glu Gln Tyr Gly Val Val Ser Ser Asn Leu  
 565 570 575

EP 1 310 571 B1

5 Gln Ser Ser Thr Ala Gly Pro Gln Thr Gln Thr Val Asn Ser Gln Gly  
580 585 590

Ala Leu Pro Gly Met Val Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly  
595 600 605

10 Pro Ile Trp Ala Lys Ile Pro His Thr Asp Gly Asn Phe His Pro Ser  
610 615 620

Pro Leu Met Gly Gly Phe Gly Leu Lys His Pro Pro Pro Gln Ile Leu  
625 630 635 640

15 Ile Lys Asn Thr Pro Val Pro Ala Asn Pro Pro Glu Val Phe Thr Pro  
645 650 655

20 Ala Lys Phe Ala Ser Phe Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser  
660 665 670

Val Glu Ile Glu Trp Glu Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn  
675 680 685

25 Pro Glu Ile Gln Tyr Thr Ser Asn Tyr Ala Lys Ser Asn Asn Val Glu  
690 695 700

30 Phe Ala Val Asn Asn Glu Gly Val Tyr Thr Glu Pro Arg Pro Ile Gly  
705 710 715 720

Thr Arg Tyr Leu Thr Arg Asn Leu  
725

35

<210> 108  
<211> 728  
<212> PRT  
40 <213> capsid protein of AAV serotype, clone 42.11

<400> 108

45 Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
1 5 10 15

Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
20 25 30

50 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
35 40 45

55 Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60



EP 1 310 571 B1

Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
100 105 110

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
115 120 125

Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
130 135 140

Pro Ile Glu Ser Pro Asp Ser Ser Thr Gly Ile Gly Lys Lys Gly Gln  
145 150 155 160

Gln Pro Ala Lys Lys Lys Leu Asn Phe Gly Gln Thr Gly Asp Ser Glu  
165 170 175

Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro Pro Ala Gly Pro Ser  
180 185 190

Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly Gly Ala Pro Met Ala  
195 200 205

Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala Ser Gly Asn Trp  
210 215 220

His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile Thr Thr Ser Thr  
225 230 235 240

Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu Tyr Lys Gln Ile  
245 250 255

Ser Ser Gln Ser Gly Ala Thr Asn Asp Asn His Phe Phe Gly Tyr Ser  
260 265 270

Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His Cys His Phe Ser  
275 280 285

Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp Gly Phe Arg Pro  
290 295 300

Arg Lys Leu Arg Phe Lys Leu Phe Asn Ile Gln Val Lys Glu Val Thr  
305 310 315 320

EP 1 310 571 B1

5 Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn Leu Thr Ser Thr Ile  
325 330 335

10 Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro Tyr Val Leu Gly Ser  
340 345 350

15 Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp Val Phe Met Ile  
355 360 365

20 Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser Gln Ser Val Gly  
370 375 380

25 Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met Leu Arg  
385 390 395 400

30 Thr Gly Asn Asn Phe Glu Phe Ser Tyr Thr Phe Glu Glu Val Pro Phe  
405 410 415

35 His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg Leu Met Asn Pro  
420 425 430

40 Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala Arg Thr Gln Ser Thr Thr  
435 440 445

45 Gly Ser Thr Arg Glu Leu Gln Phe His Gln Ala Gly Pro Asn Thr Met  
450 455 460

50 Ala Glu Gln Ser Lys Asn Trp Leu Pro Gly Pro Cys Tyr Arg Arg Gln  
465 470 475 480

55 Arg Leu Ser Lys Asp Ile Asp Ser Asn Asn Asn Ser Asn Phe Ala Trp  
485 490 495

Thr Gly Ala Thr Lys Tyr His Leu Asn Gly Arg Asn Ser Leu Thr Asn  
500 505 510

Pro Gly Val Ala Met Ala Thr Asn Lys Asp Asp Glu Asp Gln Phe Phe  
515 520 525

Pro Ile Asn Gly Val Leu Val Phe Gly Lys Thr Gly Ala Ala Asn Lys  
530 535 540

Thr Thr Leu Glu Asn Val Leu Met Thr Ser Glu Glu Glu Ile Lys Thr  
545 550 555 560

Thr Asn Pro Val Ala Thr Glu Glu Tyr Gly Val Val Ser Ser Asn Leu  
565 570 575

# EP 1 310 571 B1

5 Gln Ser Ser Thr Ala Gly Pro Gln Thr Gln Thr Val Asn Ser Gln Gly  
 580 585 590  
 Ala Leu Pro Gly Met Val Trp Gln Asn Arg Asp Val Tyr Leu Gln Gly  
 595 600 605  
 10 Pro Ile Trp Ala Lys Ile Pro His Thr Asp Gly Asn Phe His Pro Ser  
 610 615 620  
 Pro Leu Met Gly Gly Phe Gly Leu Lys His Pro Pro Pro Gln Ile Leu  
 625 630 635 640  
 15 Ile Lys Asn Thr Pro Val Pro Ala Asn Pro Pro Glu Val Phe Thr Pro  
 645 650 655  
 20 Ala Lys Phe Ala Ser Phe Ile Thr Gln Tyr Ser Thr Gly Gln Val Ser  
 660 665 670  
 Val Glu Ile Glu Trp Glu Leu Gln Lys Glu Asn Ser Lys Arg Trp Asn  
 675 680 685  
 25 Pro Glu Ile Gln Tyr Thr Ser Asn Tyr Ala Lys Ser Asn Asn Val Glu  
 690 695 700  
 30 Phe Ala Val Asn Asn Glu Gly Val Tyr Thr Glu Pro Arg Pro Ile Gly  
 705 710 715 720  
 Thr Arg Tyr Leu Thr Arg Asn Leu  
 725  
 35  
 <210> 109  
 <211> 729  
 <212> PRT  
 40 <213> capsid protein of AAV serotype, clone F1VP1  
 <400> 109  
 45 Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
 1 5 10 15  
 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
 20 25 30  
 50 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
 35 40 45  
 Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
 50 55 60  
 55 Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
 65 70 75 80

EP 1 310 571 B1

Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
 85 90 95  
 5  
 Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
 100 105 110  
 10  
 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
 115 120 125  
 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
 130 135 140  
 15  
 Pro Ile Asp Ser Pro Asp Ser Ser Thr Gly Ile Gly Lys Lys Gly Gln  
 145 150 155 160  
 20  
 Gln Pro Ala Lys Lys Lys Leu Asn Phe Gly Gln Thr Gly Asp Ser Glu  
 165 170 175  
 Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro Pro Ala Ala Pro Ser  
 180 185 190  
 25  
 Ser Val Gly Ser Gly Thr Met Ala Ala Gly Gly Gly Ala Pro Met Ala  
 195 200 205  
 30  
 Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala Ser Gly Asn Trp  
 210 215 220  
 His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile Thr Thr Ser Thr  
 225 230 235 240  
 35  
 Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu Tyr Lys Gln Ile  
 245 250 255  
 40  
 Ser Ser Ser Ser Ser Gly Ala Thr Asn Asp Asn His Tyr Phe Gly Tyr  
 260 265 270  
 Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His Cys His Phe  
 275 280 285  
 45  
 Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp Gly Phe Arg  
 290 295 300  
 50  
 Pro Lys Lys Leu Arg Phe Lys Leu Phe Asn Ile Gln Val Lys Glu Val  
 305 310 315 320  
 Thr Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn Leu Thr Ser Thr  
 325 330 335  
 55

EP 1 310 571 B1

Val Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro Tyr Val Leu Gly  
340 345 350

5 Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp Val Phe Met  
355 360 365

10 Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser Gln Ser Val  
370 375 380

Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met Leu  
385 390 395 400

15 Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr Ser Phe Glu Asp Val Pro  
405 410 415

20 Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg Leu Met Asn  
420 425 430

Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala Arg Thr Gln Ser Thr  
435 440 445

25 Thr Gly Ser Thr Arg Glu Leu Gln Phe His Gln Ala Gly Pro Asn Thr  
450 455 460

30 Met Ala Glu Gln Ser Lys Asn Trp Leu Pro Gly Pro Cys Tyr Arg Gln  
465 470 475 480

Gln Gly Leu Ser Lys Asn Leu Asp Phe Asn Asn Asn Ser Asn Phe Ala  
485 490 495

35 Trp Thr Ala Ala Thr Lys Tyr His Leu Asn Gly Arg Asn Ser Leu Thr  
500 505 510

40 Asn Pro Gly Ile Pro Met Ala Thr Asn Lys Asp Asp Glu Asp Gln Phe  
515 520 525

Phe Pro Ile Asn Gly Val Leu Val Phe Gly Lys Thr Gly Ala Ala Asn  
530 535 540

45 Lys Thr Thr Leu Glu Asn Val Leu Met Thr Ser Glu Glu Glu Ile Lys  
545 550 555 560

50 Thr Thr Asn Pro Val Ala Thr Glu Glu Tyr Gly Val Val Ser Ser Asn  
565 570 575

Leu Gln Pro Ser Thr Ala Gly Pro Gln Ser Gln Thr Ile Asn Ser Gln  
580 585 590

55

# EP 1 310 571 B1

Gly Ala Leu Pro Gly Met Val Trp Gln Asn Arg Asp Val Tyr Leu Gln  
 595 600 605  
 5  
 Gly Pro Ile Trp Ala Lys Ile Pro His Thr Asp Gly Asn Phe His Pro  
 610 615 620  
 10  
 Ser Pro Leu Met Gly Gly Phe Gly Leu Lys His Pro Pro Pro Gln Ile  
 625 630 635 640  
 15  
 Leu Ile Lys Asn Thr Pro Val Pro Ala Asn Pro Pro Glu Val Phe Thr  
 645 650 655  
 Pro Ala Lys Phe Ala Ser Phe Ile Thr Gln Tyr Ser Thr Gly Gln Val  
 660 665 670  
 20  
 Ser Val Glu Ile Glu Trp Glu Leu Gln Lys Glu Asn Ser Lys Arg Trp  
 675 680 685  
 25  
 Asn Pro Glu Ile Gln Tyr Thr Ser Asn Tyr Ala Lys Ser Asn Asn Val  
 690 695 700  
 Glu Phe Ala Val Asn Pro Asp Gly Val Tyr Thr Glu Pro Arg Pro Ile  
 705 710 715 720  
 30  
 Gly Thr Arg Tyr Leu Pro Arg Asn Leu  
 725

<210> 110

<211> 729

<212> PRT

<213> capsid protein of AAV serotype, clone F5VP1@3

<400> 110

EP 1 310 571 B1

Met Ala Ala Asp Gly Tyr Leu Pro Asp Trp Leu Glu Asp Asn Leu Ser  
1 5 10 15

5 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
20 25 30

10 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60

15 Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

20 Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
85 90 95

EP 1 310 571 B1

5 Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
 100 105 110  
 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
 115 120 125  
 10 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
 130 135 140  
 Pro Ile Asp Ser Pro Asp Ser Ser Thr Gly Ile Gly Lys Lys Gly Gln  
 145 150 155 160  
 15 Gln Pro Ala Lys Lys Lys Leu Asn Phe Gly Gln Thr Gly Asp Ser Glu  
 165 170 175  
 20 Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro Pro Ala Ala Pro Ser  
 180 185 190  
 Ser Val Gly Ser Gly Thr Met Ala Ala Gly Gly Gly Ala Pro Thr Ala  
 195 200 205  
 25 Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala Ser Gly Asn Trp  
 210 215 220  
 30 His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile Thr Thr Ser Thr  
 225 230 235 240  
 Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu Tyr Lys Gln Ile  
 245 250 255  
 35 Ser Ser Ser Ser Ser Gly Ala Thr Asn Asp Asn His Tyr Phe Gly Tyr  
 260 265 270  
 40 Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His Cys His Phe  
 275 280 285  
 Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp Gly Phe Arg  
 290 295 300  
 45 Pro Lys Lys Leu Arg Phe Lys Leu Phe Asn Ile Gln Val Lys Glu Val  
 305 310 315 320  
 50 Thr Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn Leu Thr Ser Thr  
 325 330 335  
 55 Val Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro Tyr Val Leu Gly  
 340 345 350



EP 1 310 571 B1

Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp Val Phe Met  
 355 360 365  
 5  
 Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn Asn Gly Ser Gln Ser Val  
 370 375 380  
 10  
 Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met Leu  
 385 390 395 400  
 Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr Ser Phe Glu Asp Val Pro  
 405 410 415  
 15  
 Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg Leu Met Asn  
 420 425 430  
 20  
 Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala Arg Thr Gln Ser Thr  
 435 440 445  
 Thr Gly Ser Thr Arg Glu Leu Gln Phe His Gln Ala Gly Pro Asn Thr  
 450 455 460  
 25  
 Met Ala Glu Gln Ser Lys Asn Trp Leu Pro Gly Pro Cys Tyr Arg Gln  
 465 470 475 480  
 30  
 Gln Arg Leu Ser Lys Asn Leu Asp Phe Asn Asn Asn Ser Asn Phe Ala  
 485 490 495  
 Trp Thr Ala Ala Thr Lys Tyr His Leu Asn Gly Arg Asn Ser Leu Thr  
 500 505 510  
 35  
 Asn Pro Gly Ile Pro Met Ala Thr Asn Lys Asp Asp Glu Asp Gln Phe  
 515 520 525  
 40  
 Phe Pro Ile Asn Gly Val Leu Val Phe Gly Lys Thr Gly Ala Ala Asn  
 530 535 540  
 Lys Thr Thr Leu Glu Asn Val Leu Met Thr Ser Glu Glu Glu Ile Lys  
 545 550 555 560  
 45  
 Thr Thr Asn Pro Val Ala Thr Glu Glu Tyr Gly Val Val Ser Ser Asn  
 565 570 575  
 50  
 Leu Gln Ser Ser Thr Ala Gly Pro Gln Ser Gln Thr Ile Asn Ser Gln  
 580 585 590  
 Gly Ala Leu Pro Gly Met Val Trp Gln Asn Arg Asp Val Tyr Leu Gln  
 595 600 605  
 55

# EP 1 310 571 B1

Gly Pro Ile Trp Ala Lys Ile Pro His Thr Asp Gly Asn Phe His Pro  
 610 615 620  
 5  
 Ser Pro Leu Met Gly Gly Phe Gly Leu Glu His Pro Pro Pro Gln Ile  
 625 630 635 640  
 10  
 Leu Ile Lys Asn Thr Pro Val Pro Ala Asn Pro Pro Glu Val Phe Thr  
 645 650 655  
 Pro Ala Lys Phe Ala Ser Phe Ile Thr Gln Tyr Ser Thr Gly Gln Val  
 660 665 670  
 15  
 Ser Val Glu Ile Glu Trp Glu Leu Gln Lys Glu Asn Ser Lys Arg Trp  
 675 680 685  
 20  
 Asn Pro Glu Ile Gln Tyr Thr Ser Asn Tyr Ala Lys Ser Asn Asn Val  
 690 695 700  
 Glu Phe Ala Val Asn Pro Asp Gly Val Tyr Thr Glu Pro Arg Pro Ile  
 705 710 715 720  
 25  
 Gly Thr Arg Tyr Leu Thr Arg Asn Leu  
 725  
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 <211> 729  
 <212> PRT  
 <213> capsid protein of AAV serotype, clone F3VP1  
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 <400> 111  
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 40  
 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
 20 25 30  
 45  
 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
 35 40 45  
 Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
 50 55 60  
 50  
 Val Asn Ala Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
 65 70 75 80  
 55  
 Gln Gln Leu Lys Ala Gly Asp Asn Pro Tyr Leu Arg Tyr Asn His Ala  
 85 90 95

EP 1 310 571 B1

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
 100 105 110  
 5  
 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
 115 120 125  
 10  
 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
 130 135 140  
 Pro Ile Gly Ser Pro Asp Ser Ser Thr Gly Ile Gly Lys Lys Gly Gln  
 145 150 155 160  
 15  
 Gln Pro Ala Lys Lys Lys Leu Asn Phe Gly Gln Thr Gly Asp Ser Glu  
 165 170 175  
 20  
 Ser Val Pro Asp Pro Gln Pro Leu Gly Glu Pro Pro Ala Ala Pro Ser  
 180 185 190  
 Ser Val Gly Ser Gly Thr Met Ala Ala Gly Gly Gly Ala Pro Met Ala  
 195 200 205  
 25  
 Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Asn Ala Ser Gly Asn Trp  
 210 215 220  
 30  
 His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val Ile Thr Thr Ser Thr  
 225 230 235 240  
 Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His Leu Tyr Lys Gln Ile  
 245 250 255  
 35  
 Ser Ser Ser Ser Ser Gly Ala Thr Asn Asp Asn His Tyr Phe Gly Tyr  
 260 265 270  
 40  
 Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn Arg Phe His Cys His Phe  
 275 280 285  
 Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn Asn Asn Trp Gly Phe Arg  
 290 295 300  
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 Pro Lys Lys Leu Arg Phe Lys Leu Leu Asn Ile Gln Val Lys Glu Val  
 305 310 315 320  
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 Thr Thr Asn Asp Gly Val Thr Thr Ile Ala Asn Asn Leu Thr Ser Thr  
 325 330 335  
 Val Gln Val Phe Ser Asp Ser Glu Tyr Gln Leu Pro Tyr Val Leu Gly  
 340 345 350  
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EP 1 310 571 B1

Ser Ala His Gln Gly Cys Leu Pro Pro Phe Pro Ala Asp Val Phe Met  
 355 360 365  
 5  
 Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asp Asn Gly Ser Gln Ser Val  
 370 375 380  
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 Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr Phe Pro Ser Gln Met Leu  
 385 390 395 400  
 Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr Ser Phe Glu Asp Val Pro  
 405 410 415  
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 Phe His Ser Ser Tyr Ala His Ser Gln Ser Leu Asp Arg Leu Met Asn  
 420 425 430  
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 Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu Ala Arg Thr Gln Ser Thr  
 435 440 445  
 Thr Gly Ser Thr Arg Glu Leu Gln Phe His Gln Ala Gly Pro Asn Thr  
 450 455 460  
 25  
 Met Ala Glu Gln Ser Lys Asn Trp Leu Pro Gly Pro Cys Tyr Arg Gln  
 465 470 475 480  
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 Gln Arg Leu Ser Lys Asn Leu Asp Phe Asn Asn Asn Ser Asn Phe Ala  
 485 490 495  
 Trp Thr Ala Ala Thr Lys Tyr His Leu Asn Gly Arg Asn Ser Leu Thr  
 500 505 510  
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 Asn Pro Gly Ile Pro Met Ala Thr Asn Lys Asp Asp Glu Asp Gln Phe  
 515 520 525  
 40  
 Phe Pro Ile Asn Gly Val Leu Val Phe Gly Lys Thr Gly Ala Ala Asn  
 530 535 540  
 Lys Thr Thr Leu Glu Asn Val Leu Met Thr Ser Glu Glu Glu Ile Lys  
 545 550 555 560  
 45  
 Thr Thr Asn Pro Val Ala Thr Glu Glu Tyr Gly Val Val Ser Ser Asn  
 565 570 575  
 50  
 Leu Gln Ser Ser Thr Ala Gly Pro Gln Ser Gln Thr Ile Asn Ser Gln  
 580 585 590  
 Gly Ala Leu Pro Gly Met Val Trp Gln Asn Arg Asp Val Tyr Leu Gln  
 595 600 605  
 55

# EP 1 310 571 B1

Gly Pro Ile Trp Ala Lys Ile Pro His Thr Asp Gly Asn Phe His Pro  
 610 615 620  
 5  
 Ser Pro Leu Met Gly Gly Phe Gly Leu Lys His Pro Pro Pro Gln Ile  
 625 630 635 640  
 10  
 Leu Ile Lys Asn Thr Pro Val Pro Ala Asn Pro Pro Glu Val Phe Thr  
 645 650 655  
 Pro Ala Lys Phe Ala Ser Phe Ile Thr Gln Tyr Ser Thr Gly Gln Val  
 660 665 670  
 15  
 Ser Val Glu Ile Glu Trp Glu Leu Gln Lys Glu Asn Ser Lys Arg Trp  
 675 680 685  
 20  
 Asn Pro Glu Ile Gln Tyr Thr Ser Asn Tyr Ala Lys Ser Asn Asn Val  
 690 695 700  
 Glu Phe Ala Val Asn Pro Asp Gly Val Tyr Thr Glu Pro Arg Pro Ile  
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 Gly Thr Arg Tyr Leu Thr Arg Asn Leu  
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30 <210> 112  
 <211> 735  
 <212> PRT  
 <213> capsid protein of AAV serotype, clone 42.6B

35 <400> 112

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EP 1 310 571 B1

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5 Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
20 25 30

10 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
35 40 45

Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60

15 Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

20 Lys Gln Leu Glu Gln Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala  
85 90 95

Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
100 105 110

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EP 1 310 571 B1

5 Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
 115 120 125  
 10 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
 130 135 140  
 15 Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile  
 145 150 155 160  
 20 Gly Lys Thr Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln  
 165 170 175  
 25 Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro  
 180 185 190  
 30 Pro Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly  
 195 200 205  
 35 Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser  
 210 215 220  
 40 Ser Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val  
 225 230 235 240  
 45 Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His  
 245 250 255  
 50 Leu Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp  
 260 265 270  
 55 Asn Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn  
 275 280 285  
 60 Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn  
 290 295 300  
 65 Asn Asn Trp Gly Phe Arg Pro Arg Lys Leu Arg Phe Lys Leu Phe Asn  
 305 310 315 320  
 70 Ile Gln Val Lys Glu Val Thr Thr Asp Asp Gly Val Thr Thr Ile Ala  
 325 330 335  
 75 Asn Asn Leu Thr Ser Thr Ile Gln Val Phe Ser Asp Ser Glu Tyr Gln  
 340 345 350  
 80 Leu Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe  
 355 360 365

EP 1 310 571 B1

Pro Ala Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn  
370 375 380

5 Asn Gly Ser Gln Ser Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr  
385 390 395 400

10 Phe Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr  
405 410 415

Thr Phe Glu Glu Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser  
420 425 430

15 Leu Asp Arg Leu Met Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu  
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20 Ala Arg Thr Gln Ser Thr Thr Gly Ser Thr Arg Glu Leu Gln Phe His  
450 455 460

Gln Ala Gly Pro Asn Thr Met Ala Glu Gln Ser Lys Asn Trp Leu Pro  
465 470 475 480

25 Gly Pro Cys Tyr Arg Gln Gln Arg Leu Ser Lys Asn Ile Asp Ser Asn  
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30 Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His Leu Asn  
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Gly Arg Asn Ser Leu Thr Asn Pro Gly Val Ala Met Ala Thr Asn Lys  
515 520 525

35 Asp Asp Glu Asp Gln Phe Phe Pro Ile Asn Gly Val Leu Val Phe Gly  
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40 Lys Thr Gly Ala Ala Asn Lys Thr Thr Leu Glu Asn Val Leu Met Thr  
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Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr Glu Glu Tyr  
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45 Gly Val Val Ser Ser Asn Leu Gln Ser Ser Thr Ala Gly Pro Gln Thr  
580 585 590

50 Gln Thr Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val Trp Gln Asn  
595 600 605

Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His Thr  
610 615 620

55



EP 1 310 571 B1

Asp Gly Asn Phe His Pro Ser Pro Leu Met Asp Gly Phe Gly Leu Lys  
625 630 635 640

5 His Pro Pro Pro Gln Ile Leu Ile Lys Asn Thr Pro Val Pro Ala Asn  
645 650 655

10 Pro Pro Glu Val Phe Thr Pro Ala Lys Phe Ala Ser Phe Ile Thr Gln  
660 665 670

Tyr Ser Thr Gly Gln Val Ser Val Glu Ile Glu Trp Glu Leu Gln Lys  
675 680 685

15 Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln Tyr Thr Ser Asn Tyr  
690 695 700

20 Ala Lys Ser Asn Asn Val Glu Phe Ala Val Asn Asn Glu Gly Val Tyr  
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Thr Glu Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu  
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<212> PRT  
<213> capsid protein of AAV serotype, clone 42.12  
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Glu Gly Ile Arg Glu Trp Trp Asp Leu Lys Pro Gly Ala Pro Lys Pro  
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40 Lys Ala Asn Gln Gln Lys Gln Asp Asp Gly Arg Gly Leu Val Leu Pro  
35 40 45

45 Gly Tyr Lys Tyr Leu Gly Pro Phe Asn Gly Leu Asp Lys Gly Glu Pro  
50 55 60

Val Asn Glu Ala Asp Ala Ala Ala Leu Glu His Asp Lys Ala Tyr Asp  
65 70 75 80

50 Lys Gln Leu Glu Gln Gly Asp Asn Pro Tyr Leu Lys Tyr Asn His Ala  
85 90 95

55 Asp Ala Glu Phe Gln Glu Arg Leu Gln Glu Asp Thr Ser Phe Gly Gly  
100 105 110

EP 1 310 571 B1

Asn Leu Gly Arg Ala Val Phe Gln Ala Lys Lys Arg Val Leu Glu Pro  
 115 120 125  
 5  
 Leu Gly Leu Val Glu Glu Gly Ala Lys Thr Ala Pro Gly Lys Lys Arg  
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 Pro Val Glu Pro Ser Pro Gln Arg Ser Pro Asp Ser Ser Thr Gly Ile  
 145 150 155 160  
 Gly Lys Thr Gly Gln Gln Pro Ala Lys Lys Arg Leu Asn Phe Gly Gln  
 165 170 175  
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 Thr Gly Asp Ser Glu Ser Val Pro Asp Pro Gln Pro Ile Gly Glu Pro  
 180 185 190  
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 Pro Ala Gly Pro Ser Gly Leu Gly Ser Gly Thr Met Ala Ala Gly Gly  
 195 200 205  
 Gly Ala Pro Met Ala Asp Asn Asn Glu Gly Ala Asp Gly Val Gly Ser  
 210 215 220  
 25  
 Ser Ser Gly Asn Trp His Cys Asp Ser Thr Trp Leu Gly Asp Arg Val  
 225 230 235 240  
 30  
 Ile Thr Thr Ser Thr Arg Thr Trp Ala Leu Pro Thr Tyr Asn Asn His  
 245 250 255  
 Leu Tyr Lys Gln Ile Ser Asn Gly Thr Ser Gly Gly Ser Thr Asn Asp  
 260 265 270  
 35  
 Asn Thr Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr Phe Asp Phe Asn  
 275 280 285  
 40  
 Arg Phe His Cys His Phe Ser Pro Arg Asp Trp Gln Arg Leu Ile Asn  
 290 295 300  
 Asn Asn Trp Gly Phe Arg Pro Lys Arg Leu Asn Phe Lys Leu Phe Asn  
 305 310 315 320  
 45  
 Ile Gln Val Lys Glu Val Thr Gln Asn Glu Gly Thr Lys Thr Ile Ala  
 325 330 335  
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 Asn Asn Leu Thr Ser Thr Ile Gln Val Phe Thr Asp Ser Glu Tyr Gln  
 340 345 350  
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 Leu Pro Tyr Val Leu Gly Ser Ala His Gln Gly Cys Leu Pro Pro Phe  
 355 360 365

EP 1 310 571 B1

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 10  
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 20  
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Pro Ala Asp Val Phe Met Ile Pro Gln Tyr Gly Tyr Leu Thr Leu Asn  
 370 375 380

Asn Gly Ser Gln Ala Val Gly Arg Ser Ser Phe Tyr Cys Leu Glu Tyr  
 385 390 395 400

Phe Pro Ser Gln Met Leu Arg Thr Gly Asn Asn Phe Glu Phe Ser Tyr  
 405 410 415

Gln Phe Glu Asp Val Pro Phe His Ser Ser Tyr Ala His Ser Gln Ser  
 420 425 430

Leu Asp Arg Leu Thr Asn Pro Leu Ile Asp Gln Tyr Leu Tyr Tyr Leu  
 435 440 445

Ala Arg Thr Gln Ser Thr Thr Gly Ser Thr Arg Gly Leu Gln Phe His  
 450 455 460

Gln Ala Gly Pro Asn Thr Met Ala Glu Gln Ser Lys Asn Trp Leu Pro  
 465 470 475 480

Gly Pro Cys Tyr Arg Gln Gln Arg Leu Ser Lys Asn Ile Asp Ser Asn  
 485 490 495

Asn Asn Ser Asn Phe Ala Trp Thr Gly Ala Thr Lys Tyr His Leu Asn  
 500 505 510

Gly Arg Asn Ser Leu Thr Asn Pro Gly Val Ala Met Ala Thr Asn Lys  
 515 520 525

Asp Asp Glu Asp Gln Phe Phe Pro Ile Asn Gly Val Leu Val Phe Gly  
 530 535 540

Lys Thr Gly Ala Ala Asn Lys Thr Thr Leu Glu Asn Val Leu Met Thr  
 545 550 555 560

Ser Glu Glu Glu Ile Lys Thr Thr Asn Pro Val Ala Thr Glu Glu Tyr  
 565 570 575

Gly Val Val Ser Ser Asn Leu Gln Ser Ser Thr Ala Gly Pro Gln Thr  
 580 585 590

Gln Thr Val Asn Ser Gln Gly Ala Leu Pro Gly Met Val Trp Gln Asn  
 595 600 605

Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp Ala Lys Ile Pro His Thr  
 610 615 620

# EP 1 310 571 B1

Asp Gly Asn Phe His Pro Ser Pro Leu Met Gly Gly Phe Gly Leu Lys  
625 630 635 640

5 His Pro Pro Pro Gln Ile Leu Ile Lys Tyr Thr Ser Asn Tyr Tyr Lys  
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10 Ser Thr Asn Val Asp Phe Ala Val Asn Thr Glu Gly Thr Tyr Ser Glu  
660 665 670

15 Pro Arg Pro Ile Gly Thr Arg Tyr Leu Thr Arg Asn Leu  
675 680 685

<210> 114

<211> 724

<212> PRT

20 <213> capsid protein of AAV serotype, clone AAV5CAP

<400> 114

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EP 1 310 571 B1

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5	Gly	Leu	Arg	Glu	Phe	Leu	Gly	Leu	Glu	Ala	Gly	Pro	Pro	Lys	Pro	Lys	
				20					25					30			
	Pro	Asn	Gln	Gln	His	Gln	Asp	Gln	Ala	Arg	Gly	Leu	Val	Leu	Pro	Gly	
10			35					40					45				
	Tyr	Asn	Tyr	Leu	Gly	Pro	Gly	Asn	Gly	Leu	Asp	Arg	Gly	Glu	Pro	Val	
		50					55					60					
15	Asn	Arg	Ala	Asp	Glu	Val	Ala	Arg	Glu	His	Asp	Ile	Ser	Tyr	Asn	Glu	
	65					70					75					80	
	Gln	Leu	Glu	Ala	Gly	Asp	Asn	Pro	Tyr	Leu	Lys	Tyr	Asn	His	Ala	Asp	
20					85					90					95		
	Ala	Glu	Phe	Gln	Glu	Lys	Leu	Ala	Asp	Asp	Thr	Ser	Phe	Gly	Gly	Asn	
				100					105					110			
25	Leu	Gly	Lys	Ala	Val	Phe	Gln	Ala	Lys	Lys	Arg	Val	Leu	Glu	Pro	Phe	
			115					120					125				
	Gly	Leu	Val	Glu	Glu	Gly	Ala	Lys	Thr	Ala	Pro	Thr	Gly	Lys	Arg	Ile	
30		130					135					140					
	Asp	Asp	His	Phe	Pro	Lys	Arg	Lys	Lys	Ala	Arg	Thr	Glu	Glu	Asp	Ser	
	145					150					155					160	
35	Lys	Pro	Ser	Thr	Ser	Ser	Asp	Ala	Glu	Ala	Gly	Pro	Ser	Gly	Ser	Gln	
					165					170					175		

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5

Gln Leu Gln Ile Pro Ala Gln Pro Ala Ser Ser Leu Gly Ala Asp Thr  
180 185 190

Met Ser Ala Gly Gly Gly Gly Pro Leu Gly Asp Asn Asn Gln Gly Ala  
195 200 205

10

Asp Gly Val Gly Asn Ala Ser Gly Asp Trp His Cys Asp Ser Thr Trp  
210 215 220

Met Gly Asp Arg Val Val Thr Lys Ser Thr Arg Thr Trp Val Leu Pro  
225 230 235 240

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Ser Tyr Asn Asn His Gln Tyr Arg Glu Ile Lys Ser Gly Ser Val Asp  
245 250 255

20

Gly Ser Asn Ala Asn Ala Tyr Phe Gly Tyr Ser Thr Pro Trp Gly Tyr  
260 265 270

Phe Asp Phe Asn Arg Phe His Ser His Trp Ser Pro Arg Asp Trp Gln  
275 280 285

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Arg Leu Ile Asn Asn Tyr Trp Gly Phe Arg Pro Arg Ser Leu Arg Val  
290 295 300

30

Lys Ile Phe Asn Ile Gln Val Lys Glu Val Thr Val Gln Asp Ser Thr  
305 310 315 320

Thr Thr Ile Ala Asn Asn Leu Thr Ser Thr Val Gln Val Phe Thr Asp  
325 330 335

35

Asp Asp Tyr Gln Leu Pro Tyr Val Val Gly Asn Gly Thr Glu Gly Cys  
340 345 350

40

Leu Pro Ala Phe Pro Pro Gln Val Phe Thr Leu Pro Gln Tyr Gly Tyr  
355 360 365

Ala Thr Leu Asn Arg Asp Asn Thr Glu Asn Pro Thr Glu Arg Ser Ser  
370 375 380

45

Phe Phe Cys Leu Glu Tyr Phe Pro Ser Lys Met Leu Arg Thr Gly Asn  
385 390 395 400

50

Asn Phe Glu Phe Thr Tyr Asn Phe Glu Glu Val Pro Phe His Ser Ser  
405 410 415

Phe Ala Pro Ser Gln Asn Leu Phe Lys Leu Ala Asn Pro Leu Val Asp  
420 425 430

55

## EP 1 310 571 B1

Gln Tyr Leu Tyr Arg Phe Val Ser Thr Asn Asn Thr Gly Gly Val Gln  
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 5  
 Phe Asn Lys Asn Leu Ala Gly Arg Tyr Ala Asn Thr Tyr Lys Asn Trp  
 450 455 460  
 10  
 Phe Pro Gly Pro Met Gly Arg Thr Gln Gly Trp Asn Leu Gly Ser Gly  
 465 470 475 480  
 Val Asn Arg Ala Ser Val Ser Ala Phe Ala Thr Thr Asn Arg Met Glu  
 485 490 495  
 15  
 Leu Glu Gly Ala Ser Tyr Gln Val Pro Pro Gln Pro Asn Gly Met Thr  
 500 505 510  
 20  
 Asn Asn Leu Gln Gly Ser Asn Thr Tyr Ala Leu Glu Asn Thr Met Ile  
 515 520 525  
 Phe Asn Ser Gln Pro Ala Asn Pro Gly Thr Thr Ala Thr Tyr Leu Glu  
 530 535 540  
 25  
 Gly Asn Met Leu Ile Thr Ser Glu Ser Glu Thr Gln Pro Val Asn Arg  
 545 550 555 560  
 30  
 Val Ala Tyr Asn Val Gly Gly Gln Met Ala Thr Asn Asn Gln Ser Ser  
 565 570 575  
 Thr Thr Ala Pro Ala Thr Gly Thr Tyr Asn Leu Gln Glu Ile Val Pro  
 580 585 590  
 35  
 Gly Ser Val Trp Met Glu Arg Asp Val Tyr Leu Gln Gly Pro Ile Trp  
 595 600 605  
 40  
 Ala Lys Ile Pro Glu Thr Gly Ala His Phe His Pro Ser Pro Ala Met  
 610 615 620  
 Gly Gly Phe Gly Leu Lys His Pro Pro Pro Met Met Leu Ile Lys Asn  
 625 630 635 640  
 45  
 Thr Pro Val Pro Gly Asn Ile Thr Ser Phe Ser Asp Val Pro Val Ser  
 645 650 655  
 50  
 Ser Phe Ile Thr Gln Tyr Ser Thr Gly Gln Val Thr Val Glu Met Glu  
 660 665 670  
 Trp Glu Leu Lys Lys Glu Asn Ser Lys Arg Trp Asn Pro Glu Ile Gln  
 675 680 685  
 55

# EP 1 310 571 B1

Tyr Thr Asn Asn Tyr Asn Asp Pro Gln Phe Val Asp Phe Ala Pro Asp  
690 695 700

5

Ser Thr Gly Glu Tyr Arg Thr Thr Arg Pro Ile Gly Thr Arg Tyr Leu  
705 710 715 720

Thr Arg Pro Leu

10

<210> 115

<211> 9

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<212> DNA

<213> DraIII restriction enzyme site

<400> 115

20

**caccacgtc**

9

<210> 116

25

<211> 28

<212> DNA

<213> AV2cas

<400> 116

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**cgcagagacc aaagttcaac tgaaacga**

28

35

<210> 117

<211> 255

<212> DNA

<213> adeno-associated virus serotype 10

40

<400> 117

**ggtaattcct ccggaaattg gcattgcgat tccacatggc tgggcgacag agtcatcacc 60**

45

**accagcaccc gaacctgggt cctgcccacc tacaacaacc acatctacaa gcaaattctcc 120**

**agcgagacag gagccaccaa cgacaaccac tacttctggct acagcacccc ctgggggtat 180**

**tttgacttta acagattcca ctgccacttt tcaccacgtg actggcagcg actcatcaac 240**

50

**aacaactggg gattc 255**

55

<210> 118

<211> 258

<212> DNA

<213> adeno-associated virus serotype 11



# EP 1 310 571 B1

<400> 118

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      agcgcttcaa cggggggccag caacgacaac cactactttg gctacagcac cccctggggg      180

10     tattttgact ttaacagatt ccactgccac ttctcaccac gtgactggca gcgactcacc      240
      aacaacaact ggggattc      258

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15 <210> 119  
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 <212> DNA  
 <213> adeno-associated virus serotype 12

20 <400> 119

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25     accagcaccg ggacttgggc cctgccccac tacaacaacc acctctacaa gcaaattctcc      120
      agccaatcgg gtgccaccaa cgacaaccac tacttcggct acagcaccgg ttgggggtat      180
      tttgatttca acagattcca ctgccatttc tcaccacgtg actggcagcg actcatcaac      240
30     aacaactggg gattc      255

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35 <210> 120  
 <211> 2205  
 <212> DNA  
 <213> adeno-associated virus serotype, clone A3.1vp1  
 <400> 120

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45

50

55

# EP 1 310 571 B1

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	cagtgggtgga agctcaaacc tggcccacca ccgccgaaac ctaaccaaca acaccgggac	120
5	gacagtaggg gtcttgtgct tcctgggtac aagtacctcg gacccttcaa cggactcgac	180
	aaaggagagc cgggtcaacga ggcagacgcc gcggccctcg agcacgacaa agcctacgac	240
	caccagctca agcaagggga caaccgtac ctcaaataca accacgcgga cgctgaattt	300
10	caggagcgtc ttcaagaaga tacgtctttc gggggcaacc tcgggcgagc agtcttccag	360
	gccaaaaaga ggggtactga gcctcttggg ctggttgagg aagctgttaa gacggctcct	420
	ggaaaaaaga gacctataga gcagtctcct gcagaaccgg actcttcctc gggcatcggc	480
15	aaatcaggcc agcagcccg ctaagaaaaga ctcaattttg gtcagactgg cgacacagag	540
	tcagtcccag accctcaacc aatcggagaa ccccccgcag cccctcttg tgtgggatct	600
	aatacaatgg cttcaggcgg tggggcacca atggcagaca ataacgaagg cgccgacgga	660
20	gtgggtaatt cctcgggaaa ttggcattgc gattccacat ggatgggcga cagagttatc	720
	accaccagca caagaacctg ggccctcccc acctacaata atcacctcta caagcaaadc	780
	tccagcgaat cgggagccac caacgacaac cactacttcg gctacagcac cccctggggg	840
25	tattttgact ttaacagatt ccaactgtcac ttctcaccac gtgactggca gcgactcatc	900
	aacaacaact ggggatttag acccaagaaa ctcaatttca agctcttcaa catccaagtc	960
30	aaggaggtca cgcagaatga tggaaccacg accatcgcca ataaccttac cagcacggtg	1020
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 caccctcctc cccagatcct gatcaaaaac acacctgtgc cagcgaatcc cgcgaccact 1980  
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 gaaatagagt gggagctgca gaaagaaaac agcaaacgct ggaaccaga aattcagtac 2100  
 acctccaact acaacaagtc ggtgaatgtg gagtttaccg tggacgcaaa cgggtgtttat 2160  
 35 tctgaacccc gccctattgg cactcgttac cttaccggga acttg 2205

#### 40 Claims

1. A method of identifying unknown adeno-associated virus (AAV) sequences in a sample suspected of containing AAV from a latent infection, said method comprising the steps of:

45 (a) subjecting the sample containing DNA to amplification via polymerase chain reaction (PCR) using a first set of primers which specifically amplify a first AAV region comprising at least 250 bp of AAV capsid nucleic acid sequences, said first region having a variable sequence flanked by at least 18 base pairs of highly conserved sequence at its 5' end and at least 18 base pairs of highly conserved sequence at its 3' end, said base pairs being highly conserved relative to an alignment of at least AAV1, AAV2, AAV3, AAV4, AAV5 and AAV6;  
 50 (b) optionally subjecting the DNA to further amplification using a second set of primers which specifically amplify a second region which comprises the first region of AAV sequences and sequences which are 5' to the first region, such that AAV 5' extension sequences which anneal to the 5' end of the AAV sequences amplified by the primers for the first region are obtained;  
 55 (c) optionally subjecting the DNA to further amplification using a third set of primers which specifically amplify a third region which comprises the first region of AAV sequences and sequences which are 3' to the first region, such that AAV 3' extension sequences which anneal to the 3' end of the AAV sequences amplified by the primers for the first region are obtained,

each of said second and third regions being predetermined based upon the alignment of the nucleic acid sequences of at least AAV1, AAV2, AAV3, AAV4, AAV5 and AAV6, and each of said regions comprising nucleic acid sequences which are highly conserved over at least 18 base pairs at the 5' end, optionally variable sequences in the middle, and sequences which are highly conserved over at least 18 base pairs at the 3' end of the sequences of the region, relative to the sequences of at least AAV1, AAV2, AAV3, AAV4, AAV5 and AAV6; and each of the sets of primers consisting of a 5' primer and a 3' primer; the presence of amplified sequences indicating the presence of an AAV in the sample, and a comparison of differences between the amplified sequences and the sequences of AAV1, AAV2, AAV3, AAV4, AAV5 and AAV6 indicating the presence of an unknown AAV.

2. A method according to claim 1, wherein the comparison comprises the step of comparing restriction enzyme patterns for the amplified sequences to restriction enzyme patterns of AAV1, AAV2, AAV3, AAV4, AAV5 and AAV6.
3. A method according to claim 1 or claim 2, wherein step (a) amplifies the full-length capsid gene.
4. A method according to any of claims 1 to 3, wherein the amplified sequences comprise the AAV capsid gene and the AAV rep gene.
5. A method according to any of claims 1 to 4, wherein the DNA has been extracted from cells, cell culture, tissue, tissue culture or biological fluids.
6. A method according to any of claims 1 to 5, wherein the first region is highly conserved over at least about 25 base pairs at the 5' end of the region, the 3' end of the region or both.
7. A method according to claim 6, wherein the first region is highly conserved over at least about 30 base pairs at the 5' end of the region, the 3' end of the region or both.
8. A method according to any of claims 1 to 7, wherein the highly conserved sequences of the first region have at least 80% identity among the aligned AAVs at the 5' end of the region, the 3' end of the region or both.
9. A method according to claim 8, wherein the highly conserved sequences of the first region have at least 90% identity among the aligned AAVs at the 5' end of the region, the 3' end of the region or both.
10. A method according to any of claims 1 to 9, wherein the variable sequences in the middle of the first region have less than 70% identity among the aligned AAVs.
11. A method according to any of claims 1 to 10, wherein the first region spans about bp 2800 to about 3200 of AAV 1, SEQ ID NO:6, and corresponding base pairs in other AAVs.
12. A method according to claim 11, wherein the first region is 257 bp spanning bp 2886 to about 3143 of AAV 1, SEQ ID NO:6, and corresponding base pairs in other AAVs.
13. A method according to any of claims 1 to 5, wherein the primers are AV1ns, having the sequence of nucleotides 1398 to 1423 of SEQ ID NO:6, and AV2cas, having the sequence of SEQ ID NO:7.
14. A method according to claim 1 or claim 2, wherein the first set of primers allows isolation of full-length adeno-associated virus capsid sequences from a sample, the first set of primers comprising a 5' primer directed to a region located in the middle of an AAV rep gene, based on a predetermined conserved region, and a 3' primer directed to a region downstream of an AAV cap gene, based on a predetermined conserved region of AAV.
15. A method according to any of claims 1 to 14, wherein the sample comprises AAV integrated into the chromosome.
16. A method according to any of claims 1 to 15, wherein the sample comprises human tissue.
17. A method according to any of claims 1 to 16, wherein the sample contains proviral AAV sequences.
18. A method according to any of claims 1 to 17, wherein the first region is a signature region.

19. A method according to any of claims 1 to 18, wherein the base pairs of the highly conserved sequences are highly conserved relative to an alignment of AAVs 1,2,3,4,5 and 6 and AAVs isolated from geese and ducks.
20. A method according to any of claims 1 to 19, wherein the variable sequence is a hypervariable sequence.
21. A method according to any of claims 1 to 20, wherein the first region comprises up to 10 kilobasepairs in length.
22. A method according to claim 21, wherein the first region comprises a 3-1 kilobase pair fragment comprising the full-length cap sequence.
23. A kit for detecting the presence of an unknown adeno-associated virus (AAV) in a sample from cellular DNA suspected of containing a latent AAV infection, said kit comprising:
  - (a) a first set of primers which specifically amplify a first region comprising 250 bp of AAV capsid nucleic acid sequences, said first region having at least 18 base pairs of highly conserved sequence at its 5' end, a variable sequence, and at least 18 base pairs of highly conserved sequence at its 3' end, said base pairs being highly conserved relative to an alignment of at least AAV1, AAV2, AAV3, AAV4, AAV5 and AAV6;
  - (b) optionally a second set of primers specific for a second region of the AAV nucleic acid sequences which comprises the first region of AAV sequences and sequences which are 5' to the first region, such that AAV 5' extension sequences which anneal to the 5' end of the AAV sequences amplified by the primers for the first region are obtained;
  - (c) optionally a third set of primers which specifically amplify a third region which comprises the first region of AAV sequences and sequences which are 3' to the first region, such that AAV 3' extension sequences which anneal to the 3' end of the AAV sequences amplified by the primers for the first region are obtained;each of said second and third regions being predetermined based upon the alignment of the nucleic acid sequences of at least AAV1, AAV2, AAV3, AAV4, AAV5 and AAV6, and each of said regions comprising nucleic acid sequences which are highly conserved over at least 18 base pairs at the 5' end, optionally variable sequences in the middle, and sequences which are highly conserved over at least 18 base pairs at the 3' end of the sequences of the region, relative to the sequences of at least AAV1, AAV2, AAV3, AAV4, AAV5 and AAV6;each of the sets of primers consisting of a 5' primer and a 3' primer, each of said primers comprising at least 15 nucleotides complementary to its respective highly conserved sequence and having exact identity with its respective highly conserved sequence over at least 5 base pairs in its 3' end.
24. A kit according to claim 23, wherein the 5' primer and/or the 3' primer comprises at least 18 nucleotides.
25. A kit according to claim 24, wherein the 5' primer and/or the 3' primer comprises 25 nucleotides.
26. A kit according to any of claims 23 to 25, wherein the 5' primer and/or the 3' primer comprises at least 9 base pairs of exact identity at its 3' end.
27. A kit according to claim 26, wherein the 5' primer and/or the 3' primer comprises at least 18 base pairs of exact identity at its 3' end.
28. A kit according to any of claims 23 to 27, wherein the first set of primers allows isolation of full-length adeno-associated virus capsid sequences from a sample, the first set of primers comprising a 5' primer directed to a region located in the middle of an AAV rep gene, based on a predetermined conserved region of AAV, and a 3' primer directed to a region downstream of an AAV cap gene, based on a predetermined conserved region of AAV.
29. A kit according to claim 23, wherein the 5' primer has a sequence comprising GCTGCGTCAACTGGACCAATGA-GAAC, which corresponds to nt 1398 to 1423 of SEQ ID NO:6.
30. A kit according to claim 23, wherein the 3' primer has a sequence comprising CGCAGAGACCAAAGTTCAACT-GAAACGA, which corresponds to the nucleotides complementary to 4462-4435 of SEQ ID NO:7.
31. A kit according to any of claims 23 to 30, wherein the sample comprises AAV integrated into the chromosome.

## Patentansprüche

1. Verfahren zur Identifizierung unbekannter Sequenzen von adeno-assoziiertem Virus (AAV) in einer Probe, von der man annimmt, daß sie von einer latenten Infektion herrührendes AAV enthält, wobei man in den folgenden Verfahrensschritten
  - (a) die DNA-haltige Probe einer Amplifikation über eine Polymerasekettenreaktion (PCR) unter Verwendung eines ersten Primersatzes, mit dem spezifisch ein mindestens 250 Bp AAV-Capsid-Nukleinsäuresequenzen umfassender erster AAV-Bereich amplifiziert wird, wobei dieser erste Bereich eine an ihrem 5'-Ende von mindestens 18 Basenpaaren hochkonservierter Sequenz und an ihrem 3'-Ende von mindestens 18 Basenpaaren hochkonservierter Sequenz flankierte variable Sequenz aufweist, wobei die Basenpaare relativ zu einer vergleichenden Anordnung von mindestens AAV1, AAV2, AAV3, AAV4, AAV5 und AAV6 hochkonserviert sind, aussetzt,
  - (b) gegebenenfalls die DNA einer weiteren Amplifikation unter Verwendung eines zweiten Primersatzes, mit dem spezifisch ein zweiter Bereich, der den ersten Bereich von AAV-Sequenzen sowie 5' zum ersten Bereich liegende Sequenzen umfaßt, amplifiziert wird, aussetzt, so daß 5'-AAV-Verlängerungssequenzen, die in einer Annealing-Reaktion an das 5'-Ende der mit den Primern für den ersten Bereich amplifizierten AAV-Sequenzen binden, erhalten werden,
  - (c) gegebenenfalls die DNA einer weiteren Amplifikation unter Verwendung eines dritten Primersatzes, mit dem spezifisch ein dritter Bereich, der den ersten Bereich von AAV-Sequenzen sowie 3' zum ersten Bereich liegende Sequenzen umfaßt, amplifiziert wird, aussetzt, so daß 3'-AAV-Verlängerungssequenzen, die in einer Annealing-Reaktion an das 3'-Ende der mit den Primern für den ersten Bereich amplifizierten AAV-Sequenzen binden, erhalten werden,

wobei der zweite und der dritte Bereich jeweils auf der Grundlage der vergleichenden Anordnung der Nukleinsäuresequenzen von mindestens AAV1, AAV2, AAV3, AAV4, AAV5 und AAV6 vorbestimmt sind und die Bereiche relativ zu den Sequenzen von mindestens AAV1, AAV2, AAV3, AAV4, AAV5 und AAV6 jeweils am 5'-Ende der Sequenzen des Bereichs über mindestens 18 Basenpaare hochkonservierte Nukleinsäuresequenzen, in der Mitte gegebenenfalls variable Sequenzen und am 3'-Ende über mindestens 18 Basenpaare hochkonservierte Sequenzen umfassen und die Primersätze jeweils aus einem 5'-Primer und einem 3'-Primer bestehen, das Vorhandensein amplifizierter Sequenzen das Vorhandensein eines AAV in der Probe anzeigt, und ein Vergleich der Unterschiede zwischen den amplifizierten Sequenzen und den Sequenzen von AAV1, AAV2, AAV3, AAV4, AAV5 und AAV6 das Vorhandensein eines unbekannten AAV anzeigt.
2. Verfahren nach Anspruch 1, wobei der Vergleich den Schritt des Vergleichens von Restriktionsenzymmustern für die amplifizierten Sequenzen mit Restriktionsenzymmustern von AAV1, AAV2, AAV3, AAV4, AAV5 und AAV6 umfaßt.
3. Verfahren nach Anspruch 1 oder 2, wobei in Schritt (a) das Capsid-Gen in voller Länge amplifiziert wird.
4. Verfahren nach einem der Ansprüche 1 bis 3, wobei die amplifizierten Sequenzen das AAV-Capsid-Gen und das AAV-rep-Gen umfassen.
5. Verfahren nach einem der Ansprüche 1 bis 4, wobei die DNA aus Zellen, Zellkultur, Gewebe, Gewebekultur oder biologischen Flüssigkeiten extrahiert wurde.
6. Verfahren nach einem der Ansprüche 1 bis 5, wobei der erste Bereich über mindestens etwa 25 Basenpaare am 5'-Ende oder/und am 3'-Ende des Bereichs hochkonserviert ist.
7. Verfahren nach Anspruch 6, wobei der erste Bereich über mindestens etwa 30 Basenpaare am 5'-Ende oder/und am 3'-Ende des Bereichs hochkonserviert ist.
8. Verfahren nach einem der Ansprüche 1 bis 7, wobei die hochkonservierten Sequenzen des ersten Bereichs unter den vergleichend angeordneten AAVs eine Identität von mindestens 80% am 5'-Ende oder/und am 3'-Ende des Bereichs aufweisen.
9. Verfahren nach Anspruch 8, wobei die hochkonservierten Sequenzen des ersten Bereichs unter den vergleichend

angeordneten AAVs eine Identität von mindestens 90% am 5'-Ende oder/und am 3'-Ende des Bereichs aufweisen.

10. Verfahren nach einem der Ansprüche 1 bis 9, wobei die variablen Sequenzen in der Mitte des ersten Bereichs unter den vergleichend angeordneten AAVs eine Identität von weniger als 70% aufweisen.

11. Verfahren nach einem der Ansprüche 1 bis 10, wobei der erste Bereich von etwa Bp 2800 bis etwa 3200 von AAV1, SEQ ID NO:6, und den entsprechenden Basenpaaren in anderen AAV reicht.

12. Verfahren nach Anspruch 11, wobei es sich bei dem ersten Bereich um 257 Bp handelt, die von Bp 2886 bis etwa 3143 von AAV1, SEQ ID NO:6, und den entsprechenden Basenpaaren in anderen AAV reichen.

13. Verfahren nach einem der Ansprüche 1 bis 5, wobei es sich bei den Primern um AV1ns mit der Sequenz der Nukleotide 1398 bis 1423 der SEQ ID NO:6 sowie um AV2cas mit der Sequenz der SEQ ID NO:7 handelt.

14. Verfahren nach Anspruch 1 oder Anspruch 2, wobei der erste Primersatz die Isolierung von Capsidsequenzen in voller Länge von adeno-assoziiertem Virus aus einer Probe gestattet, wobei der erste Primersatz einen auf einen in der Mitte eines AAV-rep-Gens liegenden Bereich auf der Grundlage eines vorbestimmten konservierten Bereichs gerichteten 5'-Primer sowie einen auf einen stromabwärts von einem AAV-cap-Gen liegenden Bereich auf der Grundlage eines vorbestimmten konservierten Bereichs von AAV gerichteten 3'-Primer umfaßt.

15. Verfahren nach einem der Ansprüche 1 bis 14, wobei die Probe in das Chromosom integriertes AAV umfaßt.

16. Verfahren nach einem der Ansprüche 1 bis 15, wobei die Probe menschliches Gewebe umfaßt.

17. Verfahren nach einem der Ansprüche 1 bis 16, wobei die Probe provirale AAV-Sequenzen enthält.

18. Verfahren nach einem der Ansprüche 1 bis 17, wobei es sich bei dem ersten Bereich um einen Signaturbereich handelt.

19. Verfahren nach einem der Ansprüche 1 bis 18, wobei die Basenpaare der hochkonservierten Sequenzen relativ zu einer vergleichenden Anordnung von AAV 1, 2, 3, 4, 5 und 6 und aus Gans und Ente isolierten AAV hochkonserviert sind.

20. Verfahren nach einem der Ansprüche 1 bis 19, wobei es sich bei der variablen Sequenz um eine hypervariable Sequenz handelt.

21. Verfahren nach einem der Ansprüche 1 bis 20, wobei der erste Bereich eine Länge von bis zu 10 Kilobasenpaaren umfaßt.

22. Verfahren nach Anspruch 21, wobei der erste Bereich ein die cap-Sequenz in voller Länge umfassendes Fragment von 3,1 Kilobasenpaaren umfaßt.

23. Kit zum Nachweis des Vorhandenseins eines unbekannten adeno-assoziierten Virus (AAV) in einer Probe aus zellulärer DNA, von der man annimmt, daß sie eine latente AAV-Infektion enthält, wobei der Kit umfaßt:

(a) einen ersten Primersatz, mit dem spezifisch ein 250 Bp AAV-Capsid-Nukleinsäuresequenzen umfassender erster AAV-Bereich amplifiziert wird, wobei dieser erste Bereich an seinem 5'-Ende mindestens 18 Basenpaare hochkonservierter Sequenz, eine variable Sequenz und an seinem 3'-Ende mindestens 18 Basenpaare hochkonservierter Sequenz aufweist, wobei die Basenpaare relativ zu einer vergleichenden Anordnung von mindestens AAV1, AAV2, AAV3, AAV4, AAV5 und AAV6 hochkonserviert sind,

(b) gegebenenfalls einen für einen zweiten Bereich der AAV-Nukleinsäuresequenzen, der den ersten Bereich von AAV-Sequenzen sowie 5' zum ersten Bereich liegende Sequenzen umfaßt, spezifischen zweiten Primersatz, so daß 5'-AAV-Verlängerungssequenzen, die in einer Annealing-Reaktion an das 5'-Ende der mit den Primern für den ersten Bereich amplifizierten AAV-Sequenzen binden, erhalten werden,

(c) gegebenenfalls einen dritten Primersatz, mit dem spezifisch ein dritter Bereich, der den ersten Bereich von AAV-Sequenzen sowie 3' zum ersten Bereich liegende Sequenzen umfaßt, amplifiziert wird, so daß 3'-AAV-Verlängerungssequenzen, die in einer Annealing-Reaktion an das 3'-Ende der mit den Primern für den ersten

Bereich amplifizierten AAV-Sequenzen binden, erhalten werden,

wobei der zweite und der dritte Bereich jeweils auf der Grundlage der vergleichenden Anordnung der Nukleinsäuresequenzen von mindestens AAV1, AAV2, AAV3, AAV4, AAV5 und AAV6 vorbestimmt sind und die Bereiche relativ zu den Sequenzen von mindestens AAV1, AAV2, AAV3, AAV4, AAV5 und AAV6 jeweils am 5'-Ende der Sequenzen des Bereichs über mindestens 18 Basenpaare hochkonservierte Nukleinsäuresequenzen, in der Mitte gegebenenfalls variable Sequenzen und am 3'-Ende über mindestens 18 Basenpaare hochkonservierte Sequenzen umfassen,

die Primersätze jeweils aus einem 5'-Primer und einem 3'-Primer bestehen, wobei jeder Primer mindestens 15 zur hochkonservierten Sequenz des jeweils anderen Primers komplementäre Nukleotide umfaßt und an seinem 3'-Ende über mindestens 5 Basenpaare eine genaue Identität mit der hochkonservierten Sequenz des jeweils anderen Primers aufweist.

24. Kit nach Anspruch 23, wobei der 5'-Primer und/oder der 3'-Primer mindestens 18 Nukleotide umfaßt.

25. Kit nach Anspruch 24, wobei der 5'-Primer und/oder der 3'-Primer mindestens 25 Nukleotide umfaßt.

26. Kit nach einem der Ansprüche 23 bis 25, wobei der 5'-Primer und/oder der 3'-Primer an seinem 3'-Ende mindestens 9 Basenpaare genauer Identität umfaßt.

27. Kit nach Anspruch 26, wobei der 5'-Primer und/oder der 3'-Primer an seinem 3'-Ende mindestens 18 Basenpaare genauer Identität umfaßt.

28. Kit nach einem der Ansprüche 23 bis 27, wobei der erste Primersatz die Isolierung von Capsidsequenzen in voller Länge von adeno-assoziiertem Virus aus einer Probe gestattet, wobei der erste Primersatz einen auf einen in der Mitte eines AAV-rep-Gens liegenden Bereich auf der Grundlage eines vorbestimmten konservierten Bereichs von AAV gerichteten 5'-Primer sowie einen auf einen stromabwärts von einem AAV-cap-Gen liegenden Bereich auf der Grundlage eines vorbestimmten konservierten Bereichs von AAV gerichteten 5'-Primer umfaßt.

29. Kit nach Anspruch 23, wobei der 5'-Primer eine GCTGCGTCAACTGGACCAATGAGAAC umfassende Sequenz aufweist, die Nt 1398 bis 1423 der SEQ ID NO:6 entspricht.

30. Kit nach Anspruch 23, wobei der 3'-Primer eine CGCAGAGACCAAAGTTCAACTGAAACGA umfassende Sequenz aufweist, die den zu 4462-4435 der SEQ ID NO:7 komplementären Nukleotiden entspricht.

31. Kit nach einem der Ansprüche 23 bis 30, wobei die Probe in das Chromosom integriertes AAV umfaßt.

## Revendications

1. Procédé pour identifier des séquences de virus associés à l'adénovirus (VAA) inconnus dans un échantillon dont on suspecte qu'il contient des VAA provenant d'une infection latente, ledit procédé comprenant les étapes :

(a) de soumission de l'échantillon contenant l'ADN à une amplification via une réaction de polymérase en chaîne (PCR) en utilisant une première série d'amorces qui amplifient spécifiquement une première région de VAA comprenant au moins 250 pb des séquences d'acides nucléiques de capsid de VAA, ladite première région présentant une séquence variable adjacente à au moins 18 paires de bases d'une séquence hautement conservée en son extrémité 5' et à au moins 18 paires de bases d'une séquence hautement conservée en son extrémité 3', lesdites paires de bases étant hautement conservées par rapport à un alignement d'au moins VAA1, VAA2, VAA3, VAA4, VAA5 et VAA6;

(b) éventuellement de soumission de l'ADN à une autre amplification en utilisant une deuxième série d'amorces qui amplifient spécifiquement une deuxième région qui comprend la première région de séquences des VAA et des séquences qui sont côté 5' par rapport à la première région, de telle manière qu'on obtient des séquences d'extension 5' de VAA qui hybrident sur l'extrémité 5' des séquences de VAA amplifiées par les amorces pour la première région ;

(c) éventuellement de soumission de l'ADN à une autre amplification utilisant une troisième série d'amorces qui amplifient spécifiquement une troisième région qui comprend la première région de séquences de VAA et



les séquences qui sont situées côté 3' par rapport à la première région, de telle manière qu'on obtient des séquences d'extension 3' de VAA qui hybrident sur l'extrémité 3' des séquences de VAA amplifiées par les amorces pour la première région,

- 5 chacune desdites deuxième et troisième régions étant prédéterminée sur base de l'alignement des séquences d'acides nucléiques d'au moins VAA1, VAA2, VAA3, VAA4, VAA5 et VAA6, et chacune desdites régions comprenant des séquences d'acides nucléiques qui sont hautement conservées sur au moins 18 paires de bases en l'extrémité 5', des séquences éventuellement variables au centre et des séquences qui sont hautement conservées sur au moins 18 paires de bases en l'extrémité 3' des séquences de la région, par rapport aux séquences d'au moins VAA1, VAA2, VAA3, VAA4, VAA5 et VAA6; et  
10 chacune des séries d'amorces étant constituée par une amorce 5' et une amorce 3';  
la présence de séquences amplifiées indiquant la présence d'un VAA dans l'échantillon et  
une comparaison des différences entre les séquences amplifiées et les séquences des VAA1, VAA2, VAA3, VAA4, VAA5 et VAA6 indiquant la présence d'un VAA inconnu.
- 15 2. Procédé selon la revendication 1, dans lequel la comparaison comprend l'étape de comparaison de modèles d'enzymes de restriction pour les séquences amplifiées à des modèles d'enzymes de restriction des VAA1, VAA2, VAA3, VAA4, VAA5 et VAA6.
- 20 3. Procédé selon la revendication 1 ou 2, dans lequel l'étape (a) amplifie toute la longueur du gène cap.
4. Procédé selon l'une quelconque des revendications 1 à 3, dans lequel les séquences amplifiées comprennent le gène cap du VAA et le gène rep du VAA.
- 25 5. Procédé selon l'une quelconque des revendications 1 à 4, dans lequel l'ADN a été extrait de cellules, d'une culture cellulaire, de tissu, d'une culture de tissu ou de fluides biologiques.
6. Procédé selon l'une quelconque des revendications 1 à 5, dans lequel la première région est hautement conservée sur au moins 25 paires de base en l'extrémité 5' de la région, en l'extrémité 3' de la région ou les deux.
- 30 7. Procédé selon la revendication 6, dans lequel la première région est hautement conservée sur au moins 30 paires de base en l'extrémité 5' de la région, en l'extrémité 3' de la région ou les deux.
8. Procédé selon l'une quelconque des revendications 1 à 7, dans lequel les séquences hautement conservées de la première région présentent une identité d'au moins 80% avec les VAA alignés en l'extrémité 5' de la région, l'extrémité 3' de la région ou les deux.
- 35 9. Procédé selon la revendication 8, dans lequel les séquences hautement conservées de la première région présentent une identité d'au moins 90% avec les VAA alignés en l'extrémité 5' de la région, l'extrémité 3' de la région ou les deux.
- 40 10. Procédé selon l'une quelconque des revendications 1 à 9, dans lequel les séquences variables au centre de la première région présentent une identité inférieure à 70% avec les VAA alignés.
- 45 11. Procédé selon l'une quelconque des revendications 1 à 10, dans lequel la première région s'étend de la paire de bases 2800 à environ 3200 du VAA 1, SEQ ID NO:6, et les paires de bases correspondantes dans les autres VAA.
12. Procédé selon la revendication 11, dans lequel la première région représente 257 paires de bases, s'étendant de la paire de bases 2886 à environ 3143 du VAA1, SEQ ID NO:6, et les paires de bases correspondantes dans les autres VAA.
- 50 13. Procédé selon l'une quelconque des revendications 1 à 5, dans lequel les amorces sont des AV1ns, présentant la séquence des nucléotides 1398 à 1423 de la SEQ ID NO:6, et des AV2cas, présentant la séquence de la SEQ ID NO:7.
- 55 14. Procédé selon la revendication 1 ou 2, dans lequel la première série d'amorces permet l'isolement de toute la longueur de séquences de capsid du virus associé à l'adénovirus d'un échantillon, la première série d'amorces comprenant une amorce 5' dirigée sur une région localisée au centre d'un gène rep du VAA, sur base d'une région prédéterminée conservée et une amorce 3', dirigée sur une région en aval d'un gène cap du VAA, basée sur une

région prédéterminée conservée du VAA.

15. Procédé selon l'une quelconque des revendications 1 à 14, dans lequel l'échantillon comprend un VAA intégré dans le chromosome.

16. Procédé selon l'une quelconque des revendications 1 à 15, dans lequel l'échantillon comprend du tissu humain.

17. Procédé selon l'une quelconque des revendications 1 à 16, dans lequel l'échantillon contient des séquences de VAA provirales.

18. Procédé selon l'une quelconque des revendications 1 à 17, dans lequel la première région est une région de signature.

19. Procédé selon l'une quelconque des revendications 1 à 18, dans lequel les paires de bases des séquences hautement conservées sont hautement conservées par rapport à un alignement des VAA 1,2,3,4,5 et 6 et des VAA isolés à partir d'oies et de canards.

20. Procédé selon l'une quelconque des revendications 1 à 19, dans lequel la séquence variable est une séquence hypervariable.

21. Procédé selon l'une quelconque des revendications 1 à 20, dans lequel la première région comprend jusqu'à 10 kilopaires de bases en longueur.

22. Procédé selon la revendication 21, dans lequel la première région comprend un fragment de 3,1 kilopaires de bases comprenant toute la longueur de la séquence du capsid.

23. Kit pour détecter la présence d'un virus associé à l'adénovirus (VAA) inconnu dans un échantillon d'ADN cellulaire dont on suspecte qu'il contient une infection latente par un VAA, ledit kit comprenant:

- (a) une première série d'amorces qui amplifient spécifiquement une première région comprenant 250 paires de bases de séquences d'acides nucléiques d'un capsid de VAA, ladite première région présentant au moins 18 paires de bases d'une séquence hautement conservée en son extrémité 5', une séquence variable et au moins 18 paires de base d'une séquence hautement conservée en son extrémité 3', lesdites paires de bases étant hautement conservées par rapport à un alignement d'au moins VAA1, VAA2, VAA3, VAA4, VAA5 et VAA6;
- (b) éventuellement une deuxième série d'amorces spécifiques d'une deuxième région des séquences d'acides nucléiques de VAA qui comprend la première région des séquences de VAA et des séquences qui se situent côté 5' par rapport à la première région, de manière à obtenir des séquences d'extension 5' des VAA qui hybrident sur l'extrémité 5' des séquences de VAA amplifiées par les amorces pour la première région ;
- (c) éventuellement une troisième série d'amorces qui amplifient spécifiquement une troisième région, qui comprend la première région de séquences de VAA et des séquences qui se situent côté 3' par rapport à la première région, de manière à obtenir des séquences d'extension 3' de VAA qui hybrident sur l'extrémité 3' des séquences de VAA amplifiées par les amorces de la première région;

chacune desdites deuxième et troisième région étant prédéterminée sur base de l'alignement des séquences d'acides nucléiques d'au moins les VAA1, VAA2, VAA3, VAA4, VAA5 et VAA6, et chacune desdites régions comprenant des séquences d'acides nucléiques qui sont hautement conservées sur au moins 18 paires de bases en l'extrémité 5', éventuellement des séquences variables au centre et des séquences qui sont hautement conservées sur au moins 18 paires de bases en l'extrémité 3' des séquences de la région, par rapport aux séquences au moins des VAA1, VAA2, VAA3, VAA4, VAA5 et VAA6;

chacune des séries d'amorces étant constituée par une amorce 5' et une amorce 3', chacune desdites amorces comprenant au moins 15 nucléotides complémentaires à sa séquence respective hautement conservée et présentant une identité exacte avec sa séquence respective hautement conservée sur au moins 5 paires de bases en son extrémité 3'.

24. Kit selon la revendication 23, dans lequel l'amorce 5' et/ou l'amorce 3' comprend au moins 18 nucléotides.

25. Kit selon la revendication 24, dans lequel l'amorce 5' et/ou l'amorce 3' comprend 25 nucléotides.

26. Kit selon l'une quelconque des revendications 23 à 25, dans lequel l'amorce 5' et/ou l'amorce 3' comprend au moins

9 paires de bases d'identité exacte en son extrémité 3'.

**27.** Kit selon la revendication 26, dans lequel l'amorce 5' et/ou l'amorce 3' comprend au moins 18 paires de bases d'identité exacte en son extrémité 3'.

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**28.** Kit selon l'une quelconque des revendications 23 à 27, dans lequel la première série d'amorces permet l'isolement de toute la longueur des séquences de capsides d'un virus associé à l'adénovirus d'un échantillon, la première série d'amorces comprenant une amorce 5' dirigée sur une région localisée au centre d'un gène rep d'un VAA, basée sur une région prédéterminée conservée d'un VAA et une amorce 3' dirigée sur une région en aval d'un gène cap d'un VAA, basée sur une région prédéterminée conservée d'un VAA.

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**29.** Kit selon la revendication 23, dans lequel l'amorce 5' présente une séquence comprenant GCTGCGTCAACTG-GACCAATGAGAAC, ce qui correspond aux nucléotides 1398 à 1423 de la SEQ ID NO:6.

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**30.** Kit selon la revendication 23, dans lequel l'amorce 3' présente une séquence comprenant CGCAGAGACCAAAGTT-CAACTGAAACGA, qui correspond aux nucléotides complémentaires à 4462-4435 de la SEQ ID NO:7.

**31.** Kit selon l'une quelconque des revendications 23 à 30, dans lequel l'échantillon comprend un VAA intégré dans le chromosome.

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